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THE OSMOTIC PRESSURE OF GLUCOSE SOLUTIONS AT 10°.[1]

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The present measurements of the osmotic pressure of glucose solutions have been made under much more satisfactory conditions than those of any previous series. It is recalled here that the earlier work was beset with certain well-defined difficulties which it was necessary to overcome before any high degree of precision could be ascribed to the results. The first of these difficulties was the phenomenon to which the name "*thermometer effects*" was given.[2] When the temperature of a solution in a closed cell rises, the solution expands more rapidly and to a greater extent than the containing vessel; and, unless the change of temperature is exceedingly slow—so slow, in fact, that the expulsion of water from the solution through the membrane can keep pace with the expansion of the cell contents, there is an abnormally high pressure created which may considerably exceed the true osmotic pressure. On the other hand,

[1] The work upon osmotic pressure which is in progress in this laboratory is aided by grants from the Carnegie Institution. The earlier papers upon the subject will be found in THIS JOURNAL, **26**, 80; **28**, 1; **29**, 173; **32**, 93; **34**, 1; **36**, 1 and 39; **37**, 324, 425 and 558; **38**, 175; **39**, 667.

[2] *Ibid.*, **34**, 23 and 92; **36**, 1.

when the temperature falls, the reverse occurs; the enclosed solution contracts more than the containing cell, and, if the water from without cannot enter with sufficient rapidity—as it usually cannot—an abnormally low pressure is observed. It has been found that in "slow" cells—*i. e.*, those whose membranes, owing to small area or great thickness, do not permit the rapid passage of water—the thermometer effects may even persist for several hours after the bath has recovered its normal temperature. It may be noted here that the effect of attempting to measure osmotic pressure by balancing against it mechanical pressure is, in one way, similar to the thermometer effects of rising bath temperatures. The pressure in the cell, owing to the slow escape of the solvent, rises, if the membrane is not ruptured, above the normal osmotic pressure. In another way, the two are dissimilar. The solution which has been subjected to an excessive mechanical pressure becomes permanently more concentrated than before, while the other recovers after a time its original concentration. The fluctuations after the cells had reached their maximum pressures which are to be observed in the published records of earlier determinations were frequently due to thermometer effects.

The necessity of maintaining a very nearly constant temperature throughout any given experiment became more and more apparent as the work progressed and much attention has therefore been given to devising the means by which this could be accomplished automatically and with certainty. The result has been the development of a somewhat complete system of temperature regulation for baths which will be described later, together with other important modifications of our method. For present purposes, it is sufficient to say that the results presented in this and in the preceding paper[1] are less affected by fluctuating bath temperatures than those of the earlier work.

A second source of error which gave much trouble in the earlier measurements of pressure was the upward displacements of the manometers and the distortion of the rubber stoppers,[2] both of which led to an increase of unknown amount in the

[1] THIS JOURNAL, **39**, 667.

[2] *Ibid.*, **36**, 23 and 50; **37**, 327, 460 and 580; **38**, 178.

capacity of the cell, and a consequent dilution of the solutions. If this had been the only source of dilution, it would be of little importance; but, since there were others, and it was necessary, for the proper correction of the results, to discriminate between dilution which occurred before and after the measurement of pressure, the difficulty was a serious one, leaving, as it sometimes did, a considerable margin of uncertainty as to the precise concentration of the solution whose pressure had been determined. The displacement of the manometer and the distortion of the stopper, however, were brought under tolerably good control immediately after the first three series of measurements had been completed, and that control has been continuously perfected, until the present results may be declared entirely free from sensible error due to the causes in question.

The third difficulty, and the most obstinate one of all, was the dilution of the solutions which occurred while the cells were being closed and opened.[1] The perplexities which result from such a dilution have been much discussed in former papers, but without entirely satisfactory results. The portion of the dilution which occurs while the cell is being closed precedes the measurement of pressure, and the result should be corrected for it; but that which occurs while the cell is being opened is subsequent to the measurement, and therefore without effect on the pressure. Unfortunately we had no means of determining how the dilution of the cell contents was to be distributed between the two periods, though we expressed the conviction that *not less* than half of it occurred while the cell was being opened. There was, under the circumstances, but one thing to do, and that was to devise means of suppressing *all dilution* of the cell contents, and this has, at last, been very nearly accomplished, as will be seen by inspecting the tabulated data contained in this, and in the preceding paper.

One important result of the suppression of practically all dilution in the cell is the definite location of the principal period of dilution. The corrective measures were directed against that portion of it which occurs while the cell is being opened, and it was found, when this had been eliminated, that nearly

[1] This Journal, **36**, 26 and 49; **37**, 328, 427, 463, 559 and 582.

all loss in concentration had disappeared. In 12 of the series of 19 measurements of pressure presented in this paper (see Table XX.) there was no loss of concentration whatever, and in the remaining 7, the largest dilution observed amounted to a correction of only 0.10 of an atmosphere in a total osmotic pressure of 21.38 atmospheres. The record was equally satisfactory in the paper[1] which preceded this, in which an account is given of 20 measurements of the osmotic pressure of cane sugar solutions at 10°. In 12 of these, there was no ascertainable loss of rotation, and in the remaining 8, the largest correction for such loss was only 0.09 atmosphere in a total osmotic pressure of 24.97 atmospheres. A part of even this loss is undoubtedly to be ascribed to inversion, since it has been shown in an earlier paper that a slight inversion of cane sugar always occurs in the osmotic cell.

Very substantial progress has also been made during the past year in the methods of calibrating, comparing, and testing the manometers, all of which has contributed materially to the exactness of the more recent results. The manometers are now filled with nitrogen instead of air, it having been found[2] that, however carefully purified the mercury may be, there is always a slow diminution of the volumes of air in a manometer. This apparent decrease of volume could be accounted for by supposing the tubes to stretch under pressure, and the question whether they do sensibly expand under the pressures to which we subject them is being investigated.

We are now prepared to give a conditional answer to a question which is often asked; namely, how closely, in our judgment, are we able to measure osmotic pressure? Unless there are constant sources of error of which we are unaware, and unless the remaining known sources of error are greater than we believe them to be, the uncertainties of our present measurements are confined to the second decimal place of the figures expressing the osmotic pressures. This opinion cannot be justified without an elaborate discussion of all the essential details of our method in its present and much altered form, but one bit of

[1] This Journal, **39**, 667.
[2] *Ibid.*, **37**, 326.

evidence of considerable value can be secured from the data contained in the present paper. It will be seen from Table XX., which gives a summary of the results, that the duplicate determinations of eight concentrations differed by only 0.01 atmosphere, while in two other cases, they differed by 0.04 atmosphere. The differences between duplicate determinations were also confined to the second decimal place throughout the series of measurements[1] of the pressure of cane sugar solutions at 10°. The possibilities of improvement are, however, not exhausted with the removal of the larger sources of error mentioned above, *i. e.*, displacement of the manometer and distortion of the stopper, thermometer effects, and dilution of the solution within the cell. There remain several minor sources of error, some well known and others suspected, which will hereafter receive attention in the order of their supposed relative importance.

Table I.

0.1 Wt. normal solution. Ex. No. 1. *Rotation:* (1) original, 5°.15; (2) at conclusion of expr., 5°.1; loss, 0.05 = 0.96 per cent. *Manometer:* No. 8; volume of nitrogen, 473.20; displacement, 0.08 mm. Cell used, B. Resistance of membrane, 187,000. *Corrections:* (1) atmospheric pressure, 0.99; (2) liquids in manometer, 0.47; (3) dilution, 0.02; (4) concentration, 0; (5) capillary depression, 0.02. Initial pressure, 2.06. Time of setting up cell, 4.00 P.M., Jan. 11, 1908.

	Temperature.		Volume	Pressure.		
Time.	Solution.	Manometer.	N_3.	Osmotic.	Gas.	Difference.
Jan. 14.						
3.00 P.M.	10°.1	11°.1	163.80	2.38	2.31	0.07
11.00 "	10°.1	10°.9	163.35	2.38	2.31	0.07
Jan. 15.						
9.00 A.M.	10°.1	10°.8	162.70	2.39	2.31	0.08
				2.38	2.31	0.07

Molecular osmotic pressure, 23.83.
Molecular gas pressure, 23.09.
Ratio of osmotic to gas pressure, 1.036.

[1] THIS JOURNAL, **39**, 667.

Table II.

0.1 Wt. normal solution. Exp. No. 2. *Rotation:* (1) original, 5°.1; (2) at conclusion of expr., 5°.1; loss, 0. *Manometer:* No. 9; volume of nitrogen, 432.90; displacement, 0.05 mm. Cell used, B. Resistance of membrane, 280,000. *Corrections:* (1) atmospheric pressure, 1.01; (2) liquids in manometer, 0.44; (3) dilution, 0; (4) concentration, 0; (5) capillary depression, 0.02. Initial pressure, 2.13. Time of setting up cell, 12.00 M., Jan. 18, 1908.

	Temperature.		Volume	Pressure.		
Time.	Solution.	Manometer.	N_2.	Osmotic.	Gas.	Difference.
Jan. 20.						
12.00 M.	10°.2	10°.4	146.58	2.37	2.31	0.06
Jan. 21.						
10.00 A.M.	10°.2	10°.8	145.52	2.40	2.31	0.09
1.00 P.M.	10°.2	11°.0	145.40	2.40	2.31	0.09
				2.39	2.31	0.08

Molecular osmotic pressure, 23.90.
Molecular gas pressure, 23.10.
Ratio of osmotic to gas pressure, 1.034.

Table III.

0.2 Wt. normal solution. Exp. No. 1. *Rotation:* (1) original, 10°.5; (2) at conclusion of expr., 10°.5; loss, 0. *Manometer:* No. 8; volume of nitrogen, 473.20; displacement, 0. Cell used, H. Resistance of membrane, 180,000. *Corrections:* (1) atmospheric pressure, 0.98; (2) liquids in manometer, 0.55; (3) dilution, 0; (4) concentration, 0; (5) capillary depression, 0.02. Initial pressure, 3.2. Time of setting up cell, 3.00 P.M., Jan. 24, 1908.

	Temperature.		Volume	Pressure.		
Time.	Solution.	Manometer.	N_2.	Osmotic.	Gas.	Difference.
Jan. 27.						
9.00 A.M.	10.°4	10°.6	91.13	4.78	4.63	0.15

Note—Only one satisfactory reading was obtained in this experiment.

Molecular osmotic pressure, 23.90.
Molecular gas pressure, 23.15.
Ratio of osmotic to gas pressure, 1.032.

Table IV.

0.2 Wt. normal solution. Exp. No. 2. *Rotation:* (1) original, 10°.5; (2) at conclusion of expr., 10°.5; loss, 0. *Manometer:* No. 9; volume of nitrogen, 432.90; displacement, 0. Cell used, B. Resistance of membrane, 220,000. *Corrections:* atmospheric pressure, 0.98; (2) liquids in manometer, 0.51; (3) dilution, 0; (4) concentration, 0; (5) capillary depression, 0.02. Initial pressure, 3.6. Time of setting up cell, 4.00 P.M., Jan. 24, 1908.

	Temperature.		Volume	Pressure.		
Time. Jan. 27.	Solution.	Manometer.	N_2.	Osmotic.	Gas.	Difference
11.00 A.M.	10°.2	10°.4	83.47	4.74	4.61	0.13

Note—As in the first experiment with the 0.2 normal solution, only one satisfactory reading was obtained.

Molecular osmotic pressure, 23.70.
Molecular gas pressure, 23.05.
Ratio of osmotic to gas pressure, 1.028.

Table V.

0.3 Wt. normal solution. Exp. No. 1. *Rotation:* (1) original, 15°.75; (2) at conclusion of expr., 15.°75; loss, 0. *Manometer:* No. 8; volume of nitrogen, 473.2; displacement, 0.02 mm. Cell used, B. Resistance of membrane, 229,000. *Corrections:* (1) atmospheric pressure, 1.01; (2) liquids in manometer, 0.65; (3) dilution, 0; (4) concentration, 0; (5) capillary depression, 0.02. Initial pressure, 4.62. Time of setting up cell, 5.00 P.M., Jan. 29, 1908.

	Temperature.		Volume	Pressure.		
Time. Jan. 31.	Solution.	Manometer.	N_2.	Osmotic.	Gas.	Difference.
9.00 A.M.	10°.0	10°.6	63.61	7.10	6.92	0.18
12.00 M.	10°.0	10°.4	63.36	7.13	6.92	0.21
3.00 P.M.	10°.0	10°.6	63.66	7.09	6.92	0.17
				7.11	6.92	0.19

Note—The duplicate of this experiment was lost.

Molecular osmotic pressure, 23.70.
Molecular gas pressure, 23.07.
Ratio of osmotic to gas pressure, 1.027.

Table VI.

0.4 Wt. normal solution. Exp. No. 1. *Rotation:* (1) original, 20°.8; (2) at conclusion of expr., 20°.8; loss, 0. *Manometer:* No. 20; volume of nitrogen, 416.72; displacement, 0. Cell used, H. Resistance of membrane, 139,000. *Corrections:* (1) atmospheric pressure, 1.01; (2) liquids in manometer, 0.57; (3) dilution, 0; (4) concentration, 0; (5) capillary depression, 0.02. Initial pressure, 5.14. Time of setting up cell, 4.00 P.M., Feb. 3, 1908.

	Temperature.		Volume	Pressure.		
Time.	Solution.	Manometer.	N_2.	Osmotic.	Gas.	Difference.
Feb. 5.						
9.00 A.M.	10°.2	10°.6	41.97	9.51	9.24	0.27
11.30 "	10°.1	10°.6	42.00	9.49	9.24	0.25
2.00 P.M.	10°.1	10°.7	42.00	9.50	9.24	0.26
				9.50	9.24	0.26

Molecular osmotic pressure, 23.75.
Molecular gas pressure, 23.10.
Ratio of osmotic to gas pressure, 1.028.

Table VII.

0.4 Wt. normal solution. Exp. No. 2. *Rotation:* (1) original, 20°.8; (2) at conclusion of expr., 20°.8; loss, 0. *Manometer:* No. 20; volume of nitrogen, 416.72; displacement, 0.09 mm. Cell used, H. Resistance of membrane, 185,000. *Corrections:* (1) atmospheric pressure, 1.02; (2) liquids in manometer, 0.57; (3) dilution, 0; (4) concentration, 0; (5) capillary depression, 0.02. Initial pressure, 6.4. Time of setting up cell, 4.00 P.M., Feb. 7, 1908.

	Temperature.		Volume	Pressure.		
Time.	Solution.	Manometer.	N_2.	Osmotic.	Gas.	Difference
Feb. 8.						
11.00 P.M.	10°.1	10°.3	41.72	9.55	9.24	0.31
Feb. 9.						
10.00 A.M.	10°.2	10°.3	41.78	9.53	9.24	0.29
				9.54	9.24	0.30

Molecular osmotic pressure, 23.85.
Molecular gas pressure, 23.10.
Ratio of osmotic to gas pressure, 1.032.

Table VIII.

0.5 Wt. normal solution. Exp. No. 1. *Rotation:* (1) original, 25°.80; (2) at conclusion of expr., 25°.80; loss, 0. *Manometer:* No. 20; volume of nitrogen, 416.72; displacement, 0. Cell used, H. Resistance of membrane, 180,000. *Corrections:* (1) atmospheric pressure, 1.02; (2) liquids in manometer, 0.58; (3) dilution, 0; (4) concentration, 0; (5) capillary depression, 0.02. Initial pressure, 8.82. Time of setting up cell, 4.00 P.M., Feb. 11, 1908.

	Temperature.		Volume N_2.	Pressure.		
Time.	Solution.	Manometer.		Osmotic.	Gas.	Difference.
Feb. 12.						
8.00 P.M.	10°.3	11°.6	33.80	11.92	11.56	0.36
Feb. 13.						
9.00 A.M.	10°.2	10°.6	33.80	11.92	11.55	0.37
12.00 M.	10°.05	10°.7	33.86	11.90	11.55	0.35
				11.91	11.55	0.36

Molecular osmotic pressure, 23.83.
Molecular gas pressure, 23.11.
Ratio of osmotic to gas pressure, 1.031.

Table IX.

0.5 Wt. normal solution. Exp. No. 2. *Rotation:* (1) original, 25°.8; (2) at conclusion of expr., 25°.8; loss, 0. *Manometer:* No. 20; volume of nitrogen, 416.72; displacement, 0.11 mm. Cell used, H. Resistance of membrane, 123,000. *Corrections:* (1) atmospheric pressure, 0.98; (2) liquids in manometer, 0.58; (3) dilution, 0; (4) concentration, 0; (5) capillary depression, 0.02. Initial pressure, 9.11. Time of setting up cell, 4.00 P.M., Feb. 14, 1908.

	Temperature.		Volume N_2.	Pressure.		
Time.	Solution.	Manometer.		Osmotic.	Gas.	Difference.
Feb. 15.						
8.00 P.M.	10°.2	11°.3	33.90	11.92	11.55	0.37
11.30 "	10°.0	10°.6	33.94	11.89	11.54	0.35
Feb. 16.						
10.00 A.M.	10°.0	10°.4	34.00	11.88	11.54	0.34
				11.90	11.54	0.36

Molecular osmotic pressure, 23.80.
Molecular gas pressure, 23.09.
Ratio of osmotic to gas pressure, 1.031.

Table X.

0.6 Wt. normal solution. Exp. No. 1. *Rotation:* (1) original, 30°.8; (2) at conclusion of expr., 30°.8; loss, 0. *Manometer:* No. 20; volume of nitrogen, 416.72; displacement, 0.06 mm. Cell used, H. Resistance of membrane, 140,000. *Corrections:* (1) atmospheric pressure, 0.98; (2) liquids in manometer, 0.59; (3) dilution, 0; (4) concentration, 0; (5) capillary depression, 0.02. Initial pressure, 11.26. Time of setting up cell, 4.00 P.M., Feb. 17, 1908.

	Temperature.		Volume	Pressure.		
Time.	Solution.	Manometer.	N_2.	Osmotic.	Gas.	Difference.
Feb. 19.						
9.00 A.M.	10°.1	10°.6	28.41	14.29	13.85	0.44
12.00 M	10°.0	11°.0	28.40	14.29	13.84	0.45
3.00 P.M.	10°.2	10°.6	28.39	14.31	13.86	0.45
				14.30	13.85	0.45

Molecular osmotic pressure, 23.83.
Molecular gas pressure, 23.08.
Ratio of osmotic to gas pressure, 1.032.

Table XI.

0.6 Wt. normal solution. Exp. No. 2. *Rotation:* (1) original, 31°.65; (2) at conclusion of expr., 31°.65; loss, 0. *Manometer:* No. 20; volume of nitrogen, 416.72; displacement, 0.27 mm. Cell used, G. Resistance of membrane, 367,000. *Corrections:* (1) atmospheric pressure, 1.01; (2) liquids in manometer, 0.58; (3) dilution, 0; (4) concentration, 0; (5) capillary depression, 0.02. Initial pressure, 8.00. Time of setting up cell, 4.00 P.M., Mar. 20, 1908.

	Temperature.		Volume	Pressure.		
Time.	Solution.	Manometer.	N_2.	Osmotic.	Gas.	Difference.
Mar. 21.						
12.00 M.	10°.0	10°.6	28.35	14.29	13.84	0.45
6.00 P.M.	10°.0	10°.9	28.31	14.31	13.84	0.47
Mar. 22.						
10.00 A.M.	10°.0	10°.3	28.28	14.32	13.84	0.48
				14.31	13.84	0.47

Molecular osmotic pressure, 23.85.
Molecular gas pressure, 23.07.
Ratio of osmotic to gas pressure, 1.034.

Table XII.

0.7 Wt. normal solution. Exp. No. 1. *Rotation:* (1) original, 35°.5; (2) at conclusion of expr., 35°.3; loss, 0°.2 = 0.56 per cent. *Manometer:* No. 11; volume of nitrogen, 407.37; displacement, 0.65 mm. Cell used, D. Resistance of membrane, 140,000. *Corrections:* (1) atmospheric pressure, 1.01; (2) liquids in manometer, 0.54; (3) dilution, 0.09; (4) concentration, 0; (5) capillary depression, 0.02. Initial pressure, 8.2. Time of setting up cell, 3.00 P.M., Mar. 2, 1908.

	Temperature.		Volume	Pressure.		
Time.	Solution.	Manometer.	N_2.	Osmotic.	Gas.	Difference.
Mar. 4.						
11.00 A.M.	10°.0	10°.7	23.91	16.68	16.16	0.52
Mar. 5.						
10.00 A.M.	10°.0	10°.3	23.91	16.68	16.16	0.52
5.00 P.M.	10°.1	11°.0	23.84	16.73	16.16	0.57
				16.70	16.16	0.54

Molecular osmotic pressure, 23.86.
Molecular gas pressure, 23.09.
Ratio of osmotic to gas pressure, 1.033.

Table XIII.

0.7 Wt. normal solution. Exp. No. 2. *Rotation:* (1) original, 35°.45; (2) at conclusion of expr., 35°.45; loss, 0. *Manometer:* No. 20; volume of nitrogen, 416.72; displacement, 0.14 mm. Cell used, G. Resistance of membrane, 500,000. *Corrections:* (1) atmospheric pressure, 1.01; (2) liquids in manometer, 0.59; (3) dilution, 0; (4) concentration, 0; (5) capillary depression, 0.02. Initial pressure, 11.43. Time of setting up cell, 6.00 P.M., Mar. 23, 1908.

	Temperature.		Volume	Pressure.		
Time.	Solution.	Manometer.	N_2.	Osmotic.	Gas.	Difference.
Mar. 24.						
11.00 P.M.	10°.1	10°.7	24.43	16.67	16.16	0.51
Mar. 25.						
9.00 A.M.	10°.0	10°.6	24.41	16.67	16.16	0.51
12.00 M.	10°.0	10°.8	24.38	16.70	16.16	0.54
4.00 P.M.	10°.0	10°.7	24.38	16.70	16.16	0.54
				16.69	16.16	0.53

Molecular osmotic pressure, 23.84.
Molecular gas pressure, 23.09.
Ratio of osmotic to gas pressure, 1.033.

Table XIV.

0.8 Wt. normal solution. Exp. No. 1. *Rotation:* (1) original, 40°.2; (2) at conclusion of expr., 40°.1; loss, 0.1=0.25 per cent. *Manometer:* No. 11; volume of nitrogen, 407.37; displacement, 0.30 mm. Cell used, D. Resistance of membrane, 367,000. *Corrections:* (1) atmospheric pressure, 1.01; (2) liquids in manometer, 0.55; (3) dilution, 0.05; (4) concentration, 0; (5) capillary depression, 0.02. Initial pressure, 16.00. Time of setting up cell, 4.00 P.M., Mar. 20, 1908.

	Temperature.		Volume	Pressure.		
Time.	Solution.	Manometer.	N_2.	Osmotic.	Gas.	Difference.
Mar. 21.						
1.00 P.M.	10°.0	10°.6	21.00	19.01	18.46	0.55
6.00 P.M.	10°.0	10°.9	20.96	19.04	18.46	0.58
11.00 P.M.	10°.15	10°.9	20.85	19.07	18.47	0.60
Mar. 22.						
10.00 A.M.	10°.0	10°.3	20.96	19.04	18.46	0.58
				19.04	18.46	0.58

Molecular osmotic pressure, 23.80.
Molecular gas pressure, 23.08.
Ratio of osmotic to gas pressure, 1.031.

Table XV.

0.8 Wt. normal solution. Exp. No. 2. *Rotation:* (1) original, 40°.1; (2) at conclusion of expr., 40°.1; loss, 0. *Manometer:* No. 20; volume of nitrogen, 416.72; displacement, 0.04 mm. Cell used D. Resistance of membrane, 190,000. *Corrections:* (1) atmospheric pressure, 1.01; (2) liquids in manometer, 0.60; (3) dilution, 0; (4) concentration, 0; (5) capillary depression, 0.02. Initial pressure, 15.14. Time of setting up cell, 1.00 P.M., Mar. 29, 1908.

	Temperature.		Volume	Pressure.		
Time.	Solution.	Manometer.	N_2.	Osmotic.	Gas.	Difference.
Mar. 30.						
4.00 P.M.	10°.0	11°.8	21.42	19.06	18.46	0.60
8.00 P.M.	10°.0	11°.7	21.44	19.05	18.46	0.59
12.00 P.M.	10°.0	11°.4	21.43	19.05	18.46	0.59
				19.05	18.46	0.59

Molecular osmotic pressure, 23.81.
Molecular gas pressure, 23.08.
Ratio of osmotic to gas pressure, 1.032.

Table XVI.

0.9 Wt. normal solution. Exp. No. 1. *Rotation:* (1) original, 44°.70; (2) at conclusion of expr., 44°.55; loss, 0°.15= 0.34 per cent. *Manometer:* No. 14; volume of nitrogen, 420.6; displacement, 0.22 mm. Cell used, D. Resistance of membrane, 150,000. *Corrections:* (1) atmospheric pressure, 1.02; (2) liquids in manometer, 0.59; (3) dilution, 0.07; (4) concentration, 0; (5) capillary depression, 0.02. Initial pressure, 13.66. Time of setting up cell, 11.30 A.M., Mar. 8, 1908.

Time.	Temperature. Solution.	Manometer.	Volume N_2.	Pressure. Osmotic.	Gas.	Difference.
Mar. 10.						
9.00 A.M.	10°.0	10°.3	19.35	21.39	20.77	0.62
12.30 P.M.	10°.1	10°.4	19.36	21.37	20.78	0.59
Mar. 11.						
8.00 A.M.	10°.2	10°.2	19.37	21.42	20.79	0.63
				21.39	20.78	0.61

Molecular osmotic pressure, 23.77.
Molecular gas pressure, 23.09.
Ratio of osmotic to gas pressure, 1.030.

Table XVII.

0.9 Wt. normal solution. Exp. No. 2. *Rotation:* (1) original, 44°.80; (2) at conclusion of expr., 44°.60; loss, 0°.20= 0.45 per cent. *Manometer:* No. 14; volume of nitrogen, 420.6; displacement, 0.42 mm. Cell used, D. Resistance of membrane, 275,000. *Corrections:* (1) atmospheric pressure, 1.00; (2) liquids in manometer, 0.59; (3) dilution, 0.10; (4) concentration, 0; (5) capillary depression, 0.02. Initial pressure, 15.87. Time of setting up cell, 4.00 P.M., Mar. 26, 1908.

Time.	Temperature. Solution.	Manometer.	Volume N_2.	Pressure. Osmotic.	Gas.	Difference.
Mar. 27.						
5.00 P.M.	10°.0	11°.1	19.41	21.38	20.77	0.61
11.00 P.M.	10°.0	10°.8	19.42	21.38	20.77	0.61
Mar. 28.						
9.00 A.M.	10°.0	10°.9	19.41	21.38	20.77	0.61
				21.38	20.77	0.61

Molecular osmotic pressure, 23.76.
Molecular gas pressure, 23.08.
Ratio of osmotic to gas pressure, 1.029.

Table XVIII.

1.0 Wt. normal solution. Exp. No. 1. *Rotation:* (1) original, 49°.15; (2) at conclusion of expr., 49°.00; loss, 0°.15= 0.3 per cent. *Manometer:* No. 14; volume of nitrogen, 420.6; displacement, 0.17 mm. Cell used, D. Resistance of membrane, 124,000. *Corrections:* (1) atmospheric pressure, 1.00; (2) liquids in manometer, 0.61; (3) dilution, 0.07; (4) concentration, 0; (5) capillary depression, 0.02. Initial pressure, 11.05. Time of setting up cell, 4.00 P.M., Mar. 16, 1908.

Time.	Temperature. Solution.	Manometer.	Volume N_2.	Pressure. Osmotic.	Gas.	Difference.
Mar. 17.						
5.00 P.M.	10°.1	11°.1	17.46	23.80	23.09	0.71
Mar. 18.						
4.00 P.M.	10°.0	10°.9	17.47	23.77	23.08	0.69
10.00 P.M.	10°.0	10°.9	17.46	23.79	23.08	0.71
Mar. 19.						
9.00 A.M.	10°.0	10°.7	17.46	23.78	23.08	0.70
				23.79	23.08	0.71

Molecular osmotic pressure, 23.79.
Molecular gas pressure, 23.08.
Ratio of osmotic to gas pressure, 1.031.

Table XIX.

1.0 Wt. normal solution. Exp. No. 2. *Rotation:* (1) original, 49°.35; (2) at conclusion of expr., 49°.15; loss, 0°.2= 0.41 per cent. *Manometer:* No. 6; volume of nitrogen, 405.34; displacement, 0.61 mm. Cell used, D. Resistance of membrane, 500,000. *Corrections:* (1) atmospheric pressure, 1.01; (2) liquids in manometer, 0.62; (3) dilution, 0.09; (4) concentration, 0; (5) capillary depression, 0.02. Initial pressure, 12.00. Time of setting up cell, 5.00 P.M., Mar. 23, 1908.

Time.	Temperature. Solution.	Manometer.	Volume N_2.	Pressure. Osmotic.	Gas.	Difference.
Mar. 24.						
11.00 P.M.	10°.1	10°.7	16.85	23.79	23.09	0.70
Mar. 25.						
9.00 A.M.	10°.0	10°.6	16.84	23.79	23.08	0.71
12.00 M.	10°.0	10°.8	16.83	23.81	23.08	0.73
4.00 P.M.	10°.0	10°.7	16.84	23.80	23.08	0.72
				23.80	23.08	0.72

Molecular osmotic pressure, 23.80.
Molecular gas pressure, 23.08.
Ratio of osmotic to gas pressure, 1.031.

Table XX.—Summary of Results.

Concentration.	Temperature.	Loss in rotation.	Correction for dilution.	Osmotic pressure.	Gas pressure.	Difference.	Molecular osmotic pressure.	Molecular gas pressure.	Ratio of osmotic to gas pressure.
0.1	10°.10	0°.05	0.02	2.38	2.31	0.07	23.83	23.09	1.036
0.1	10°.20	0°.00	0.00	2.39	2.31	0.08	23.90	23.10	1.034
0.2	10°.40	0°.00	0.00	4.78	4.63	0.15	23.90	23.15	1.032
0.2	10°.20	0°.00	0.00	4.74	4.61	0.13	23.70	23.05	1.028
0.3	10°.00	0°.00	0.00	7.11	6.92	0.19	23.70	23.07	1.027
0.4	10°.10	0°.00	0.00	9.50	9.24	0.26	23.75	23.10	1.028
0.4	10°.15	0°.00	0.00	9.54	9.24	0.30	23.85	23.10	1.032
0.5	10°.20	0°.00	0.00	11.91	11.55	0.36	23.83	23.11	1.031
0.5	10°.10	0°.00	0.00	11.90	11.54	0.36	23.80	23.09	1.031
0.6	10°.10	0°.00	0.00	14.30	13.85	0.45	23.83	23.08	1.032
0.6	10°.00	0°.00	0.00	14.31	13.84	0.47	23.85	23.07	1.034
0.7	10°.00	0°.20	0.09	16.70	16.16	0.54	23.86	23.09	1.033
0.7	10°.00	0°.00	0.00	16.69	16.16	0.53	23.84	23.09	1.033
0.8	10°.05	0°.10	0.05	19.04	18.46	0.58	23.80	23.08	1.031
0.8	10°.00	0°.00	0.00	19.05	18.46	0.59	23.81	23.08	1.032
0.9	10°.10	0°.15	0.07	21.39	20.78	0.61	23.71	23.09	1.030
0.9	10°.00	0°.20	0.10	21.38	20.77	0.61	23.76	23.08	1.029
1.0	10°.00	0°.15	0.07	23.79	23.08	0.71	23.79	23.08	1.031
1.0	10°.00	0°.20	0.09	23.80	23.08	0.72	23.80	23.08	1.031

Table XXI.—Summary of Results—Mean Values.

Concentration.	Temperature.	Loss in rotation.	Correction for dilution.	Osmotic pressure.	Gas pressure.	Difference.
0.1	10°.15	0°.03	0.01	2.39	2.31	0.08
0.2	10°.30	0°.00	0.00	4.76	4.62	0.14
0.3	10°.00	0°.00	0.00	7.11	6.92	0.19
0.4	10°.10	0°.00	0.00	9.52	9.24	0.28
0.5	10° 15	0°.00	0.00	11.91	11.55	0.36
0.6	10°.05	0°.00	0.00	14.31	13.85	0.46
0.7	10°.00	0°.10	0.05	16.70	16.16	0.54
0.8	10°.00	0°.05	0.03	19.05	18.46	0.59
0.9	10°.05	0°.18	0.09	21.39	20.78	0.61
1.0	10°.00	0°.18	0.09	23.80	23.08	0.72

Concentration.	Temperature.	Molecular osmotic pressure.	Molecular gas pressure.	Ratio of osmotic to gas pressure.
0.1	10°.15	23.87	23.10	1.035
0.2	10°.30	23.80	23.10	1.030
0.3	10°.00	23.70	23.07	1.027
0.4	10°.10	23.80	23.10	1.030
0.5	10°.15	23.82	23.10	1.031
0.6	10°.05	23.84	23.08	1.033
0.7	10°.00	23.85	23.09	1.033
0.8	10°.00	23.81	23.08	1.032
0.9	10°.05	23.74	23.09	1.030
1.0	10°.00	23.80	23.08	1.031
		23.80	23.09	1.031

The conclusions to be drawn from the data contained in Tables I. to XIX., and summarized in Tables XX. and XXI., are:

1. That at 10° the osmotic pressure of glucose solutions is proportional to the concentration. This is best illustrated by means of the molecular pressures. The mean molecular pressure of the whole ten concentrations (see Table XXI.) is 23.80 atmospheres, while the highest and the lowest molecular pressures for the individual concentrations are 23.87 and 23.70 atmospheres, respectively. In respect to the proportionality of pressure to concentration, glucose behaves at 10° precisely as it was found to conduct itself at 0° and in the vicinity of 20°. It will be recalled that the freezing point depressions of glucose

solutions are also strictly proportional to their weight-normal concentration.

2. That the excess of osmotic over gas pressure which was observed in the neighborhood of 0° has not disappeared at 10°. The mean molecular osmotic pressure at the temperature employed in this series of measurements is 23.80 atmospheres, while the mean molecular gas pressure is 23.09. The comparison is best made by means of the ratios given in the last column of Table XXI. It will there be seen that the mean ratio of osmotic to gas pressure, for all concentrations between 0.1 and 1.0 weight-normal solutions, is, at 10°, 1.031, while the maximum and minimum ratios for the individual concentrations are respectively 1.035 and 1.027. At 10° the osmotic pressure of glucose solutions is about 3.0 per cent higher than the gas pressure. At 0° the excess of osmotic over gas pressure was found to be about 5.0 per cent.

3. That the closer approximation of osmotic to gas pressure at 10° than at 0° is due in greater measure to the increase in gas pressure between these temperatures than to the augmentation of osmotic pressure. The mean molecular gas pressure at the temperatures around 0°, at which the former measurements were made, was 22.28 atmospheres, while for the present series of measurements around 10°, it is 23.09—an increase of 0.81 atmosphere. The mean molecular osmotic pressure at the lower temperature was found to be 23.45 atmospheres. At 10°, as noted above, it is 23.80—an increase of only 0.35 atmosphere. From evidence in hand we are inclined to believe that when we repeat the work at 0° under the better conditions which now prevail, we shall find a molecular osmotic pressure of about 23.36 atmospheres. If so, the increase between 0° and 10° will be 0.46 instead of 0.35 atmosphere. It appears that the increase in the osmotic pressure of glucose solutions from 0° to 10° is only about half as fast as the increase in gas pressure between those temperatures.

The first series of measurements of the osmotic pressure of glucose solutions was made at temperatures between 21°.7 and 26°.9. The mean ratio of osmotic to gas pressure at these temperatures was found to be 0.993, while the mean of the molecu-

lar osmotic pressures was 24.01 atmospheres, the mean molecular gas pressure being 24.19 atmospheres. The first series of measurements was, however, made under disadvantageous conditions. The means of regulating temperature were much less satisfactory than at present, the displacements of the manometers had not at that time been brought under good control, and dilution of the cell contents from other causes had not been suppressed. There was an average loss of rotation of 1.49 per cent, for all of which the results were corrected. We know now that some of this must have occurred while the cells were being opened and subsequent to the measurements of pressure. It is therefore probable that later work will modify for this series, by some fraction of 1.49 per cent, the osmotic gas ratio of 0.993, and, correspondingly, the mean molecular osmotic pressure of 24.01.

Below is given a tabular statement of the osmotic gas ratios and the mean molecular osmotic pressures thus far found for glucose solutions. Each series covers all the concentrations from 0.1 to 1.0 weight-normal.

	Temperatures.	Mean ratio of osmotic to gas pressure.	Mean molecular osmotic pressures.
Series I.	21°.7–26°.9	0.993	24.01 atmospheres.
" III.	10°.0	1.031	23.80 "
" II.	0°.0	1.052	23.45 "

The values for series III. will not, we think, be much modified by later investigation, but those of series I. and II. will probably be slightly altered, the former by some fraction of 1.49 per cent, and the latter by some fraction of 0.90 per cent—these numbers representing the average amount of the dilution which was observed in those series, regarding the proper correction for which some uncertainty still exists.

JOHNS HOPKINS UNIVERSITY,
April 25, 1908.

[Contributions from the Sheffield Laborotory of Yale University.]

CLVI. RESEARCHES ON PYRIMIDINES. THE ACTION OF NITRIC ACID ON 2,6-DIOXYPYRIMIDINES. OXYNITROHYDROTHYMINE.

[THIRTIETH PAPER.]

By Treat B. Johnson.

I shall describe, in this paper, some results which I have obtained by examining the behavior of fuming nitric acid towards 5-bromuracil, 5-chloruracil, and synthetical thymine.

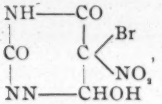
In a paper entitled "Die Constitution des Thymins,"[1] Steudel has described the action of concentrated nitric acid on thymine. He obtained a compound to which he assigned the empirical formula $C_4H_4O_3N_4$. He gave no melting point for the compound, but states that it did not contain water of crystallization, that it was soluble in warm water and ammonia, and gave, on reduction, a derivative which responded to Weidel's alloxan reaction. I have repeated Steudel's experiment and have investigated the action of nitric acid of different concentrations and under various conditions, but in no case have I obtained a compound identical with his *nitrothymine*. The data which I have obtained seem to indicate that Steudel's *nitrothymine* was a secondary decomposition product, and not a simple thymine derivative.

Uracil, 5-bromuracil, 5-chloruracil, and thymine do not react, below 100°, with nitric acid of density 1.41. On the other hand, uracil dissolves, at ordinary temperature, in fuming nitric acid (sp. gr. 1.5), giving a good yield of 5-nitrouracil (I.). 5-Bromuracil, 5-chloruracil, and thymine react, under the same conditions, giving three derivatives corresponding to the empirical formulas II., III., and IV., respectively. The same compound IV. was also obtained when thymine was treated with concentrated nitric acid according to the directions of Steudel.[2]

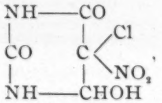
Uracil, $C_4H_4O_2N_2 \longrightarrow C_4H_3O_2N_2(NO_2)$, I. (5-Nitrouracil).
5-Bromuracil, $C_4H_3O_2N_2(Br) \longrightarrow C_4H_3O_2N_2(Br)HNO_3$, II.
5-Chloruracil, $C_4H_3O_2N_2(Cl) \longrightarrow C_4H_3O_2N_2(Cl)HNO_3$, III.
Thymine, $C_4H_3O_2N_2(CH_3) \longrightarrow C_4H_3O_2N_2(CH_3)HNO_3$, IV.

[1] Z. physiol. Chem., **32**, 241.
[2] *Loc. cit.*

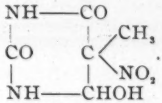
I now find that the compound II., prepared from 5-bromuracil and nitric acid, is identical with *bromnitrooxyhydrouracil*, V., which Behrend[1] obtained by treatment of nitrouracil with bromine water. This interesting result, and the fact that the analogous compounds, III. and IV., are prepared under the same conditions, indicate that they have a similar structure and are to be considered as oxynitrohydropyrimidines; *viz.*, chlornitrooxyhydrouracil, VI., and oxynitrohydrothymine, VII., respectively:



V.

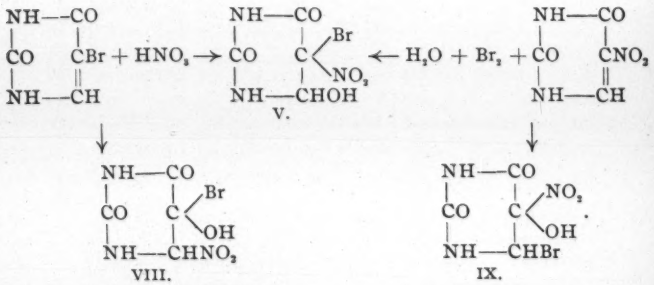


VI.



VII.

The formation of these hydropyrimidines involves a direct addition of nitric acid to the double bond between the 4 and 5 positions of the pyrimidine ring. The preparation of bromnitrooxyhydrouracil, V., from 5-nitrouracil and 5-bromuracil shows that the nitro group and bromine atom are linked to the same carbon atom. It also proves Behrend's[2] original conclusion that the formation of oxyhydropyrimidines, from certain pyrimidines, by the action of chlorine and bromine water involves an addition of hypochlorous and hypobromous acids at the double bond.



V.

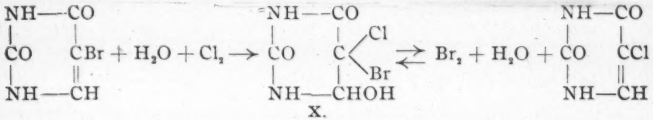
VIII.

IX.

[1] Ann. Chem. (Liebig), **240**, 11.

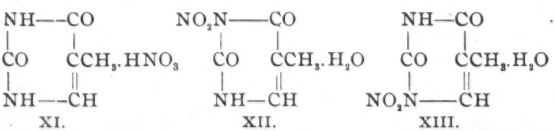
[2] Ann. Chem. (Liebig), **229**, 20.

I also find that 5-bromuracil and 5-chloruracil react with chlorine water and bromine water, respectively, giving the same chlorbromoxyhydrouracil, X. When this hydropyrimidine was digested with alcohol it was converted into 5-chloruracil.

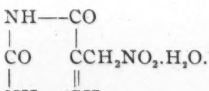


X.

Thymine apparently shows no tendency to form salts with acids. It can be crystallized from concentrated hydriodic and hydrobromic acids without alteration. The possibility of the nitro derivative IV. being a nitric acid salt, XI. is excluded since thymine is not formed by treatment with alkalis, and also because it does not react with bromine water to give oxybromhydrothymine.[1] The compound is not a substituted nitro derivative, as represented by formulas XII., XIII., and XIV., because it does not contain water of crystallization. It can be crystallized repeatedly from absolute alcohol without alteration.



XI. XII. XIII.

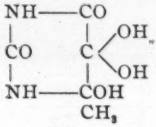


XIV.

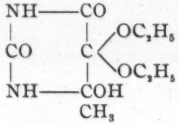
I have made the interesting observation that oxynitrohydrothymine, VII., can exist in two modifications which I have designated by the Greek letters α and β. The two isomers are obtained under practically the same conditions. The α derivative is the stable modification and melts at 183°–185°. The β derivative melts at 230°–235° and rearranges to the α form at

[1] Jones: Z. physiol. Chem., **29**, 20.

ordinary temperature. The two isomers are especially characterized by their crystalline habit and are converted quantitatively into thymine when reduced with tin and hydrochloric acid. This interesting case of isomerism is possibly similar in nature to that recently observed by Osten.[1] He found, for example, that methylisodialuric acid, XV., and its diethyl ether, XVI., occur in two isomeric modifications which undergo reversible transformations in the presence of acids and alkalis.

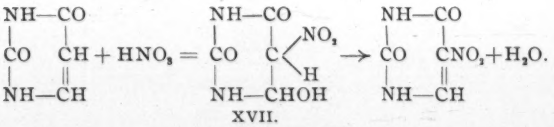


XV.



XVI.

Oxynitrohydropyrimidines are probably formed in every case when 5-nitropyrimidines are obtained by the action of nitric acid. For example: the formation of nitrouracil from uracil probably involves an addition of nitric acid, giving the unstable hydropyrimidine XVII., which then breaks down with loss of a molecule of water, giving nitrouracil. In the case of thymine, on the other hand, the molecule cannot lose water in the normal manner and therefore the intermediate hydropyrimidine, VII., is capable of isolation.

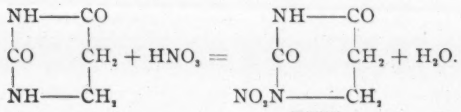


XVII.

It is interesting to note here the behavior of nitric acid towards hydrouracil.[2] This compound contains no double bond between the 4 and 5 positions and the 5 position is not the point of attack. It reacts with nitric acid, giving a nitro derivative, XVIII., in which the nitro group is linked to the 3 position of the pyrimidine ring.

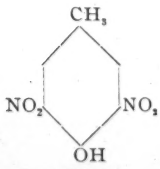
[1] Ann. Chem. (Liebig), **343**, 133.

[2] Franchimont and Friedmann: Rec. trav. chim., **26**, 218.

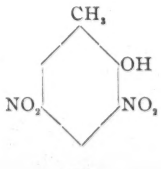


XVIII.

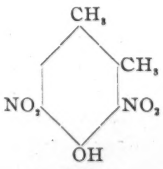
The isolation of the above oxynitrohydropyrimidines lends new interest to some early observations on the action of nitric acid on certain benzene derivatives. For example: nitric acid reacts with toluene, in presence of sulphuric acid, giving 3, 5-dinitroparacresol, XIX., and 3,5-dinitroorthocresol, XX.[1] Orthoxylene gives a mixture of 3,5-dinitroparaxylenol, XXI., and 3,5-dinitroorthoxylenol,[2] XXII. Orthocresolsulphonic acid reacts with nitric acid, giving 3,5-dinitroorthocresol,[3] XX. Similar observations have also been made in the naphthalene series.[4] Armstrong explains these abnormal reactions by assuming an addition of nitric acid to a double bond in the benzene ring, giving unstable addition products. These then break down in two ways, either with separation of nitrous acid, giving a phenol, or with loss of water, giving a nitro derivative.



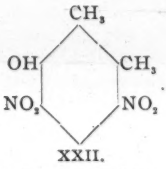
XIX.



XX.



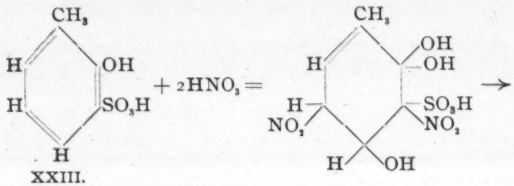
XXI.



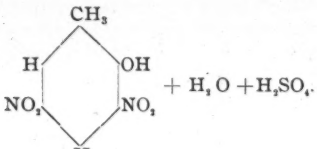
XXII.

[1] Nolting and Forel: Ber. d. chem. Ges., **18**, 2670.
[2] Nolting and Pick: *Ibid.*, **21**, 3158.
[3] Claus and Jackson: J. prakt. Chem. (2), **38**, 333.
[4] Armstong and Rossiter: P. Chem. Soc., **1891**, 87–89; Ber. d. chem. Ges., **24**, R. 721.

The action of nitric acid on orthocresolsulphonic acid, XXIII., may be represented by the following equation. The writer is not aware that such intermediate addition products with nitric acid have been isolated in the benzene series.



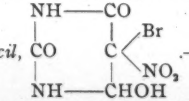
XXIII.



XX.

EXPERIMENTAL PART.

The Action of Nitric Acid (sp. gr. 1.5) on 5-Bromuracil.



Oxynitrobromhydrouracil, —This compound was first described by Behrend.[1] I prepared it in the following manner: Three grams of finely pulverized 5-bromuracil were dissolved in 19 cc. of nitric acid and the solution allowed to evaporate in a vacuum over sulphuric acid. I obtained 3.3 grams of the pure hydropyrimidine which crystallized in large blocks and rectangular prisms. The pyrimidine had no definite melting point, but decomposed from 150° to 165° according to the rate of heating. It was difficultly soluble in cold water but could not be purified by recrystallization from this solvent. When warmed with water above 40° it was decomposed with

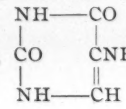
[1] *Loc. cit.*

formation of brompicrin, which was recognized by its disagreeable odor. The pyrimidine did not contain water of crystallization. It agreed in its chemical behavior, so far as I was able to judge, with the hydropyrimidine described by Behrend.

0.3006 gram of substance gave 0.2204 gram CO_2 and 0.0481 gram H_2O. Nitrogen (Kjeldahl).

	Calculated for $C_4H_4O_3N_2Br$.	Found. I.	II.
C	19.00	20.00	...
H	1.57	1.77	...
N	16.53	...	16.35

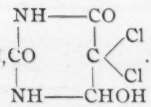
Reduction of Oxynitrobromhydrouracil with Tin and Hydrochloric Acid.—Two grams of the hydropyrimidine were reduced, on the steam bath, for one hour with an excess of tin and hydrochloric acid. The solution was then evaporated to dryness to remove the excess of hydrochloric acid and the residue redissolved in water. The tin was then removed by precipitation with hydrogen sulphide and the filtrate concentrated to a volume of 20 cc. Five grams of potassium cyanate were then added to the solution when I obtained an insoluble, granular precipitate. The compound was difficultly soluble in hot water and practically insoluble in the common organic solvents and dilute sulphuric acid. It did not contain halogens, and left no inorganic residue when burned on a platinum foil. When the compound was warmed with bromine water and then treated with an excess of barium hydroxide solution, a purple precipitate was obtained. Its characteristic properties and nitrogen determinations identified the compound as Behrend's[1] *hydroxyxanthine*,



Nitrogen (Kjeldahl):

	Calculated for $C_5H_4O_2N_4$.	Found. I.	II.
N	32.94	32.80	32.95

[1] Ann. Chem. (Liebig), **229**, 40; **240**, 6.

Oxydichlorhydrouracil,  .H_2O.—This compound was prepared by dissolving uracil in an excess of strong chlorine water, or by oxidizing uracil with potassium chlorate and dilute hydrochloric acid. Five grams of finely pulverized uracil were suspended in about 100 cc. of chlorine water and chlorine gas conducted into the solution until the pyrimidine had dissolved. The excess of chlorine was then removed with a current of air and the solution concentrated on the steam bath. On cooling, prismatic crystals of chloruracil (see below) deposited. These were removed by filtration and the filtrate concentrated further. The hydropyrimidine then separated, on cooling, in the form of tables melting at 205°–208° with effervescence. In a second experiment 2 grams of uracil were dissolved in 80 cc. of 20 per cent hydrochloric acid and the solution heated to 70°–90°. Potassium chlorate was then occasionally added in small portions and the oxidation continued at 50°–60° for four hours. The excess of chlorine was then removed in the usual manner and the solution allowed to stand. The oxydichlorhydrouracil finally separated in stout prisms which decomposed at 208°–210°. The hydropyrimidine crystallized from water in large, well-developed prisms melting at 212°–215° with effervescence. Aqueous solutions of the pyrimidine gave a purple precipitate when warmed with a solution of barium hydroxide. The pyrimidine was recovered unaltered after boiling with alcohol for 24 hours. The corresponding dibrom derivative[1] is converted into 5-bromuracil by the same treatment. Oxydichlorhydrouracil contained one molecule of water of crystallization which was determined by heating for one hour at 100°–110°.

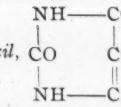
0.9157 gram of substance lost 0.0778 gram of H_2O.

	Calculated for $C_4H_4O_3N_2Cl_2.H_2O$.	Found.
H_2O	8.30	8.49

Nitrogen determination for hydrous pyrimidine (Kjeldahl):

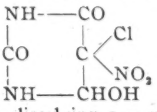
	Calculated for $C_4H_4O_3N_2Cl_2.H_2O$.	Found.
N	12.90	12.67

[1] Wheeler and Johnson: J. Biol. Chem., **3**, 183.



5-Chloruracil, —This compound was always obtained associated with oxydichlorhydrouracil when uracil was treated with chlorine water. It can be prepared by reducing the hydropyrimidine with tin and hydrochloric acid. The pyrimidine separated from the acid solution in the form of rectangular prisms and square tables. It was practically insoluble in alcohol and cold water. It crystallized from hot water in prisms melting at 300°–305° according to the rate of heating. The pyrimidine did not contain water of crystallization. Nitrogen (Kjeldahl):

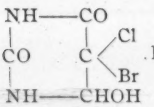
	Calculated for $C_4H_3O_2N_2Cl$.	Found. I.	II.	III.
N	19.11	19.03	19.5	19.00



Oxynitrochlorhydrouracil, . $1\frac{1}{2}H_2O$. — This pyrimidine was prepared by dissolving 1.0 gram of 5-chloruracil in 10 cc. of fuming nitric acid (sp. gr. 1.5). When the solution was allowed to evaporate spontaneously, in the atmosphere, the pyrimidine separated in hard, prismatic crystals. The substance had no definite melting point but decomposed with effervescence from 150° to 160°, according to the rate of heating. It slowly underwent decomposition when heated at 100°–110° and was also decomposed by boiling water. The compound contained water of crystallization (Analysis I.), which it slowly lost when exposed to the atmosphere. After drying over sulphuric acid, in a desiccator, for 6 days, the analytical determination agreed with the calculated value for the anhydrous material (Analyses II. and III.). (Kjeldahl):

	Calculated for $C_4H_4O_5N_3Cl.1\frac{1}{2}H_2O$.	Found. I.
N	17.75	17.7

	Calculated for $C_4H_4O_5N_3Cl$.	Found. II.	III.
N	20.04	19.57	19.6

Oxychlorbromhydrouracil,  H_2O.—This pyrimidine can be prepared from 5-bromuracil or 5-chloruracil by dissolving them in an excess of chlorine water and bromine water, respectively. It was very soluble in water and crystallized from bromine water in prismatic crystals, decomposing at 195°–200°, with effervescence. It reacted with barium hydroxide, in aqueous solution, giving a purple precipitate. The pyrimidine contained one molecule of water of crystallization, which was determined by heating for one hour at 90°–110°. The compound slowly loses its water of crystallization in the atmosphere and becomes anhydrous after standing for several hours in a desiccator over sulphuric acid.

I. 0.7413 gram substance lost 0.0516 gram H_2O.

II. 0.2029 gram substance lost 0.0123 gram H_2O.

	Calculated for $C_4H_4O_3N_2ClBr.H_2O$.	Found. I.	II.
H_2O	6.88	6.95	6.50

Nitrogen determination for hydrous pyrimidine (Kjeldahl):

	Calculated for $C_4H_4O_3N_2ClBr.H_2O$.	Found.
N	10.70	10.66

Nitrogen determination for anhydrous pyrimidine (Kjeldahl):

	Calculated for $C_4H_4O_3N_2ClBr$.	Found. I.	II.
N	11.49	11.31	11.4

Action of Boiling Alcohol on Oxychlorbromhydrouracil.—Five-tenths of a gram of the hydropyrimidine, melting at 195°–200°, was dissolved in 20 cc. of absolute alcohol and the solution boiled for ten hours. The alcohol was then removed by evaporation and the product obtained was crystallized from hot water. It separated in stout prisms, decomposing at 300°–305°. It gave a test for chlorine and a mix-

ture of the compound and 5-chloruracil decomposed sharply at 300°–305°. Analysis (Kjeldahl):

	Calculated for $C_4H_3O_2N_2Cl$.	Calculated for $C_4H_3O_2N_2Br$.	Found.
N	19.11	14.66	19.04

Action of Bromine Water on 5-Iodouracil.—5-Iodouracil was decomposed by bromine water with liberation of iodine. About 1 gram of the pyrimidine was dissolved in bromine water, and the solution allowed to evaporate spontaneously in the atmosphere. Transparent prisms finally separated, which decomposed sharply at 200°–205°. The compound did not contain iodine, but gave a strong test for bromine. It was converted into 5-bromuracil when heated with absolute alcohol. A nitrogen determination agreed with the calculated value for oxydibromhydrouracil[1] (Kjeldahl):

	Calculated for $C_4H_4O_3N_2Br_2$.	Found.
N	9.72	9.6

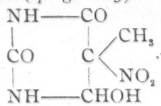
The Action of Nitric Acid on Thymine.

Nitric Acid (sp. gr. 1.415).—Five-tenths of a gram of thymine was dissolved in 2 cc. of concentrated nitric acid and the solution evaporated to dryness on the steam bath. There was no evidence of any reaction and the thymine was recovered unaltered. It deposited from hot water in plates that decomposed at about 321°. When mixed with pure thymine this decomposition point was not lowered.

Analysis (Kjeldahl):

	Calculated for $C_5H_6O_2N_2$.	Found.
N	22.22	22.23

Nitric Acid (sp. gr. 1.5). The Formation of α-Oxynitrohydrothymine,



.—Thymine dissolves in cold, fuming nitric acid with slight evolution of heat. If red fumes are evolved by this treatment it is a safe indication that the

[1] Wheeler and Johnson: *Loc. cit.*

thymine is not pure. The hydropyrimidine was obtained perfectly pure, and the yield was quantitative, when thymine was treated with fuming nitric acid under the following conditions: One gram of thymine was dissolved in 6 cc. of nitric acid and the solution allowed to evaporate at ordinary temperature. The nitro derivative deposited in large, well-developed prisms or blocks, which decrepitated above 130° and melted at 183° with violent effervescence. The compound was soluble in hot water, extremely soluble in alcohol, and separated from both these solvents in blocks that melted at 183°–185°. It was practically insoluble in benzene. The pyrimidine did not lose weight after heating for 1.5 hours at 100°–110° and again for one-half hour at 110°–115°. When heated above 120° it slowly underwent decomposition. The composition of the compound was not altered by recrystallization from absolute alcohol (Analysis III.).

0.2086 gram substance gave 0.2454 gram CO_2 and 0.0695 gram H_2O.

Nitrogen (Kjeldahl):

	Calculated for $C_5H_7O_5N_3$.	Calculated for $C_5H_6O_2N_2$.	Found. I.	II.	III.
C	31.74	47.61	32.08	...	...
H	3.70	4.76	3.70	...	...
N	22.22	22.22	...	22.00	21.95

α-Oxynitrohydrothymine dissolves in water, giving an acid reaction. The pyrimidine undergoes decomposition when its aqueous solution is boiled. The addition of barium hydroxide to its aqueous solution produces no precipitate or color; also no thymine deposited when an alcoholic solution of the pyrimidine was treated with ammonia. When the nitropyrimidine was dissolved in concentrated sulphuric acid, and a few drops of ferrous sulphate solution were added, the characteristic test for nitric acid was obtained. α-Oxynitrohydrothymine can also be prepared by dissolving thymine in fuming nitric acid (sp. gr. 1.5) and evaporating the solution to dryness, at once, on the steam bath. This method of nitration can be recommended for preparing quickly small quantities of the hydropyrimidine. The yields are not quan-

titative, since part of the thymine undergoes oxidation. The best results are obtained when 1 gram portions are nitrated under the following conditions: One gram of thymine is dissolved in 4 cc. of nitric acid (sp. gr. 1.5) and the solution evaporated to dryness as quickly as possible. The nitrothymine is obtained as a colorless, crystalline residue which separates from water in blocks decomposing at 183°–185°. It is possible, in this manner, to prepare several grams of the hydropyrimidine in a few minutes. The yields obtained by this method of nitration were very uniform and are given in the table below.

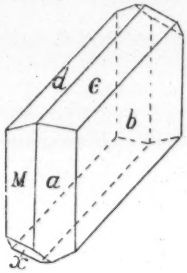
Number.	Nitric acid, sp. gr. 1.5. Cc.	Weight of thymine. Grams.	Weight of crude oxynitrohydrothymine. Grams.	Weight of hydropyrimidine after crystallization from water. M. p. 183°-185°. Grams.	Per cent of theoretical of pure hydrothymine.
1	4	1	1.1	0.80	57.1
2	4	1	1.1	0.82	58.5
3	4	1	1.1	0.79	56.4
4	4	1	1.1	0.81	57.8
5	8	2	2.15	1.60	55.5
6	4	1	1.2	0.90	64.4
7	8	2	2.1	1.50	53.5

Crystallography of Oxynitrohydrothymine.

By W. E. Ford.

The pyrimidine crystallizes in the triclinic system, showing a combination of *b* (010), *c* (001), *a* (100), *M* (110), *d* (034) and *X* (111). The crystals were small, averaging about 2 mm. broad by 1 mm. thick. In habit they present the appearance of diamond-shaped tables with beveled edges, as is illustrated in the figure. The face, *b* (010), is always the most prominent, while the prism with the pinacoid, *a*, and the base with the dome, *d*, form the beveling faces. Frequently one of these latter faces is much subordinated in size, or may be entirely wanting. The negative pyramid, *X*, is always small, and often not present. The crystal faces, although distinct to the eye, were very poorly adapted for measurement with

the reflection goniometer. They were usually quite rough or curved and gave indistinct and broad signals on the goniometer. A series of the crystals was measured on the two-circle goniometer, and the average of the best readings ob-



tained was taken for the fundamental angles, but the angles as given and the crystallographic constants calculated from them can be considered only as proximate. The measured angles were as follows:

(010) : (110) = 63°54′.
(010) : (100) = 96°15′.
(010) : (001) = 73°38′.
Zone (010) . (110) : Zone (010) . (001) = 79°35′.
Zone (010) . (110) : Zone (010) . (101) = 50°5′.
(010) : (034) = 71°33′; calc. = 71°46′.

Using the first five measurements as fundamentals, the crystal constants were calculated to be

$a:b:c = 0.578:1.000:0.420$. $\alpha = 107°35'$, $\beta = 100°25'$, $\gamma = 80°59'$.

The crystals show a good cleavage parallel to *c* (001). On account of the nature of the material only a few of the optical facts concerning the compound could be determined. It possesses a strong double refraction. The extinction direction on *b* (010) is inclined to the edge between *b* and *a* at 31°. The crystals, when looked at in the polariscope in a direction

perpendicular to *c* (001), the cleavage face, show the emergence of an optic axis nearly in the center of the field.

Action of Nitric Acid (sp. gr. 1.5) in Presence of Concentrated Sulphuric Acid.—There was an immediate reaction, with evolution of red fumes, when 0.5 gram of thymine was dissolved in a mixture of 3 cc. of nitric and 3 cc. of sulphuric acids. When the mixture was allowed to stand, without cooling, the reaction continued to increase in violence, with evolution of heat, and the thymine was completely decomposed. In a second experiment, 1 gram of thymine was dissolved in a cold mixture of 3 cc. nitric and 2 cc. concentrated sulphuric acids. This solution was held at a temperature of 70°–75° for about three-quarters of an hour, when gas bubbles had practically ceased to be formed. The acid solution was then cooled and poured into 15 cc. of ice water. After standing for several hours, stout, well-developed prisms deposited from the solution. They melted at 183°–185°, with effervescence, and were identified as *oxynitrohydrothymine*. They were soluble in alcohol and warm water. Analysis (Kjeldahl):

	Calculated for $C_5H_7O_6N_3$.	Found.
N	22.22	21.66

Action of Bromine Water on α-Oxynitrohydrothymine.—One gram of the hydropyrimidine was dissolved in an excess of bromine water and the solution allowed to evaporate spontaneously. There was no evidence of a reaction and oxynitrohydrothymine separated in large, transparent blocks melting at 183°–185°.

Analysis (Kjeldahl):

	Calculated for $C_5H_7O_6N_3$.	Found.
N	22.22	22.42

Reduction of α-Oxynitrohydrothymine with Aluminum Amalgam.—Two and five-tenths grams of the hydrothymine were dissolved in cold water and reduced for 1.5 hours with an excess of aluminum amalgam. The temperature was not allowed to rise above 40° during the reduction. After fil-

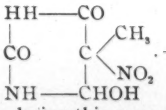
tering from aluminum amalgam and aluminum hydroxide the filtrate was evaporated to dryness. I obtained a crystalline deposit which was difficultly soluble in cold water, but separated from hot water in plates melting at 320°. When mixed with thymine the melting point was not lowered. It dissolved in fuming nitric acid, giving the original *α-oxynitrohydrothymine* melting at 183°–185°. Analysis (Kjeldahl):

	Calculated for $C_5H_6O_5N_2$.	Found.
N	22.22	22.01

Reduction of α-Oxynitrohydrothymine with Tin and Hydrochloric Acid.—Two and two-tenths grams of the hydropyrimidine were reduced for one hour with an excess of tin and concentrated hydrochloric acid. The acid solution was then evaporated to dryness, the residue dissolved in water, and the tin removed by precipitation with hydrogen sulphide. When the aqueous filtrate was concentrated and cooled, thymine separated in glistening plates, decomposing at 320°. Analysis (Kjeldahl):

	Calculated for $C_5H_6O_2N_2$.	Found.
N	22.22	22.10

β-Oxynitrohydrothymine,



.—I have performed fifteen experiments, during this research, to determine the behavior of fuming nitric acid towards thymine under different conditions. I have taken different amounts of thymine (0.5–5.0 grams), and have varied the proportions of nitric acid. I have also allowed the acid solution to evaporate under different conditions—at room temperature, on the steam oven, in a vacuum over sulphuric acid, and at 100°—but in only two experiments have I observed the formation of *β-oxynitrohydrothymine*. The conditions under which I obtained this isomer were as follows: One and six-tenths grams of thymine were dissolved in 8 cc. of cold, fuming nitric acid (sp. gr. 1.5) and the solution was allowed to evaporate

in the atmosphere overnight. The following morning large, transparent blocks had deposited, which showed no signs of melting at 183°–185°, but decomposed at 230°–235°, according to the rate of heating. One of the crystals selected for analysis weighed 0.2600 gram. The isomer did not revert to the α derivative when crystallized from water or absolute alcohol, but separated, on cooling, in well-developed prisms decomposing at 230°–236°. In another experiment, 0.5 gram of thymine was dissolved in 10 cc. of fuming nitric acid and the solution allowed to evaporate over sulphuric acid in a vacuum desiccator. I obtained practically a quantitative yield of the β derivative melting at 230°-235°. The compound did not lose weight when heated for one-half hour at 90°–100°. Analysis (Kjeldahl):

	Calculated for $C_5H_7O_5N_3$.	Found. I.	II.
N	22.22	22.00	22.1

Reduction of β-Oxynitrohydrothymine with Tin and Hydrochloric Acid.—This compound was reduced in the same manner as the α derivative. The excess of tin was removed with hydrogen sulphide and the filtrate evaporated to dryness. I obtained a crystalline residue which separated from water in plates melting at 315°–320°. The compound sublimed when heated in a test tube, and when mixed with thymine, the melting point was not lowered. It dissolved in fuming nitric acid, giving *α-oxynitrohydrothymine* melting at 183°–185°. Analysis (Kjeldahl):

	Calculated for $C_5H_6O_5N_2$.	Found.
N	22.22	22.31

Rearrangement of β-Oxynitrohydrothymine into α-Oxynitrohydrothymine.—Some of the α-pyrimidine, melting at 183°–185°, was preserved in a desiccator from May 29, 1907, until January 17, 1908. It apparently underwent no change, and melted at 181°–183° with effervescence. A sample of the β-pyrimidine, melting at 230°–235°, was preserved from June 19, 1907, to October 7, 1907. It then decomposed at 227°–235°, and a nitrogen determination (Kjeldahl) gave 22.00

per cent; calculated, 22.22 per cent nitrogen. This material was not examined again until January 16, 1908. It then had completely rearranged to the α-pyrimidine and melted at 183°–188° with effervescence. A mixture of this material and pure α-oxynitrohydrothymine melted at 183°–186° with effervescence. Analysis (Kjeldahl):

	Calculated for $C_5H_7O_3N_3$.	Found.
N	22.22	21.9

I take pleasure in thanking Professor W. E. Ford for the crystallographic description of oxynitrohydrothymine and also Mr. D. B. Jones for his help in this investigation.

NEW HAVEN, CONN.,
Jan. 18, 1908.

[Contribution from the Kent Chemical Laboratory of the University of Chicago.]

THE "SYN" AND "ANTI" STEREOISOMERISM OF NITROGEN COMPOUNDS.

BY JULIUS STIEGLITZ.

In 1903,[1] in the course of an investigation with R. B. Earle on the cause of the rearrangement of the metal salts of acid chlor- and bromamides, RC(:N Hal)OMe, a long search for stereoisomeric esters, RC(N:NCl)OR′, corresponding in structure to the above salts, resulted in the discovery of the first known pair of such stereoisomers in the form of two methyl chlorimido-*m*-nitrobenzoates, $NO_2C_6H_4C(:NCl)OCH_3$. The investigation of such stereoisomers has been continued since then by myself in collaboration with W. J. Hale, Oscar Eckstein, and Willis S. Hilpert; the conclusions drawn in the preliminary report have been confirmed in every detail and a large amount of additional evidence obtained, supplementing the results obtained in the first place. In a later paper the work done with the stereoisomeric esters on the question of the theory of the "Beckmann rearrangement" will be discussed; in this paper it is intended to consider only the question of the new class of stereoisomers, whose existence has

[1] THIS JOURNAL, **30**, 399 (1903).

been fully established, and their relation to the general question of stereoisomerism of nitrogen compounds.

I. Stereoisomeric Chlorimidoesters.

The following pairs of stereoisomeric chlorimidoesters have now been prepared in this laboratory, the physical and chemical differences of the two compounds forming each pair being briefly summarized:

1. α- and β-Methyl chlorimido-m-nitrobenzoates,[1]

$$NO_2C_6H_4C(=NCl)OCH_3 \quad \text{and} \quad NO_2C_6H_4C(=ClN)OCH_3,$$

were prepared with Earle and are described in the preliminary report. Hilpert[2] has improved the method of preparation and of separation of the two bodies, so that they are now very easily obtained. The α compound forms needles melting at 88° and is less soluble in chloroform and ligroin than is the β compound. It does not lose its identity when subjected to the various forms of physical transformation; recrystallization from various solvents, fusion and solidification, moderate heat (150°), do not change it into the other form. Under the influence of dry chlorine (see IV., below) it is transformed into the more stable β compound.

The β compound forms thick prisms melting at 84°, is much more soluble in ligroin and chloroform than the α body, and also preserves its identity through all forms of physical changes. It is much the more stable of the two stereoisomers, is formed in larger proportion, and is obtained from the α body by the action of chlorine, as stated above; but the β compound is also transformed by the same agent to a slight extent into the α compound, the reaction being reversible, as proved by Dr. Hilpert.

A mixture of equal quantities of the two pure stereoisomers melts at 63°–65°, the melting point being depressed some 20°.

[1] The prefix *a* was uniformly given to the higher melting stereoisomer. See below, Part V., in regard to the configurations of the compounds.

[2] A report by Dr. Hilpert will appear in a later number of THIS JOURNAL. I wish to take this occasion to thank Dr. Hilpert, my chief collaborator in the study of these stereoisomers, for his thorough and skilful work.

2. α- and β-Ethyl chlorimido-m-nitrobenzoates, $NO_2C_6H_4C(:NCl)OC_2H_5$, were prepared with Dr. Hale. The α compound, crystallizing in long, flat needles and melting at 63°, is formed in largest quantity and is the more stable of the two stereoisomers, in contrast to the relations for the methyl esters. In all other respects it resembles the α compound of the methyl ester pair. The β compound crystallizes in small, striated prisms, melts at 52°, and is formed in very small quantities. Dry chlorine converts it into the α body.

3. α- and β-Methyl chlorimido-p-nitrobenzoates, *p*-$NO_2C_6H_4C(:NCl)OCH_3$, were prepared by Hilpert,[1] as were all the succeeding stereoisomers. The α compound resembles the α compound of the meta series in its appearance, stability, and behavior; it forms needles melting at 99°–100°. The β form appears as thick prisms, melts at 76°, is the more soluble and the more stable stereoisomer of the two. Chlorine converts the α compound readily into the β form, but the latter is also to some extent converted into the less stable α form by the same agent. A mixture of the two stereoisomers melts at about 60°.

4. α and β- Ethyl chlorimido-p-nitrobenzoates,[1] *p*-$NO_2C_6H_4C(:NCl)OC_2H_5$, are entirely analogous to the stereoisomeric *ethyl* esters of the meta series—particularly also in regard to the striking fact that here again the α compound (needles, m. p. 96°) is so much the more stable that the β body (plates, m. p. 90°) could be obtained (0.5 gram) only by weeks of patient collecting of single crystals. A mixture of the two bodies melts at about 72°.

5. α- and β-Methyl m-Nitro-p-methylbenzoates,[2] *m*-NO_2-*p*-$CH_3C_6H_3C(NCl)OCH_3$.—The higher melting α compound (m. p. 84°–85°) forms plates, is the less soluble, but also the less stable, isomer, forming the β compound under the influence of chlorine. The β compound forms needles, which melt at 71°, and is the more stable form. A mixture of the two melts at 53°–54°. Except for the noteworthy change of crystal forms, the two stereoisomers conform en-

[1] *Loc. cit.*
[2] *Ibid.*

tirely in their properties to the corresponding α and β compounds of the other stereoisomeric *methyl* esters.

6. α- and β-Methyl Chlorimido-β-naphthoates,[1] β-$C_{10}H_7C(NCl)OCH_3$.—All the stereoisomers hitherto described have been nitro derivatives, the nitro group being used to raise the melting points of the esters and to facilitate somewhat their separation by fractional crystallization. The chlorimidoesters of β-naphthoic acid were prepared in the hope that they would also be solid and that we could isolate stereoisomers which would have no nitro group in the molecule. This hope was realized. The α compound forms needles, melts at 125°, and is much the less soluble of the two. The β compound forms thin plates melting at 72°. A mixture of the two compounds melts at 66°–67°. There is not much difference in the stability of the stereoisomers, they can be converted one into the other by treatment with hot water.[1] They are stable towards physical changes and do not lose their identity.

7. α- and β-Ethyl Chlorimido-β-naphthoates,[1] β-$C_{10}H_7C(NCl)OC_2H_5$.—The α compound is the less soluble, crystallizes in thin lamellae looking like needles, and melts at 72°. The β compound was probably not isolated but its existence was rigorously proved in a compound melting at 39°, which, by analysis, represented perfectly pure ethyl chlorimidonaphthoate and for which identity of structure with that of the α body, *i. e.*, as an ethyl chlorimido-β-naphthoate, was proved.[1] The body melting at 39° is considered to be a saturated mixture of the α and β forms, because its melting point was not depressed by the addition of some pure α compound (m. p. 72°). It is certain that it contains a compound with the same composition and same structure as the α body, but different from it and therefore stereoisomeric with it.

II. The Proof of Identical Structure for each Pair of Stereoisomers.

The rigorous proof of the identity of structure for the two

[1] Hilpert: Loc. cit.

compounds forming each pair of stereoisomers, $RC(:NCl)OR$,[1] was, of course, considered of prime importance, especially in view of the fact that structural isomerism in the acid radical R, in regard to the position of the substituting nitro groups, etc., and isomerism in regard to the position of the alkyl radical R′ had to be excluded.

The identity of structure of the pairs of stereoisomers was in each case proved in the following direct way; each stereoisomer, its purest preparation being always used, was treated in ligroin solution with dry hydrogen chloride, reduction to the hydrochloride of the mother substance, the imidoester, being effected as follows:

$$RC(:NCl)OR' + 2HCl \longrightarrow RC(:NH_2Cl)OR' + Cl_2.$$

The identity of the imidoester salt formed was established in two ways: (1) The dry imidoester hydrochlorides break down, when heated, into an acid amide and an alkyl chloride, according to the formulation

$$RC(:NH_2Cl)OR' \longrightarrow RCONH_2 + R'Cl.$$

The acid amide thus obtained from each stereoisomer was not only examined in regard to its own melting point, but, the melting points of the acid amide prepared from a pair of stereoisomers being always found exactly the same, a melting point of a mixture of the two preparations was also taken and found to be the same as that of the individual amides. This evidence brought conclusive proof of the identity of the acid radical R in each pair of stereoisomers.

(2) The imidoester salts break down under the influence of water into esters and ammonium chloride, according to the formulation

$$RC(NH_2Cl)OR' + H_2O \longrightarrow RCOOR' + NH_4Cl.$$

Each of a pair of stereoisomeric chlorimidoesters always gave the same acid ester (methyl *m*-nitrobenzoate, methyl *p*-nitrobenzoate, etc.), as the other one of the pair did, the identity of the ester being proved by the rigorous method described for the acid amides. This proved the identity of

[1] Hilpert: *Loc. cit.*

the groups OR′ and of the acid radicals R in the pairs of stereoisomers and completed the proof of their structure.

Corroborative evidence of the identity of the structures or the pairs of stereoisomers was found as follows: (3) For the original pair of stereoisomers, methyl chlorimido-*m*-nitrobenzoate, the isomeric compound, *m*-nitrobenzchlormethylamide, $NO_2C_6H_4CO(NClCH_3)$, containing the methyl group attached to nitrogen and not to oxygen, was prepared by Stieglitz and Earle and found to be different from the two stereoisomers.[1] (4) The derivatives obtained from *p*-nitrobenzoic acid are quite different in their physical constants from those obtained from *m*-nitrobenzoic acid. (5) The smooth and rapid transformation of one stereoisomer into its more stable mate by the action of chlorine or hot water (see IV.) precludes any structural difference in the groups R and R′ and is exactly what is to be expected of such stereoisomers.

III. The Physical Behavior.

Molecular weight determinations by the cryoscopic method were made in benzene solution with three pairs of stereoisomers, the methyl chlorimido-*m*-nitrobenzoates, the methyl *p*-methyl-*m*-nitrobenzoates, and the methyl chlorimidonaphthoates. They proved beyond cavil that the two members of a pair have the same molecular weight, the possibility of polymerism being thus excluded.

Physical or crystal isomerism was rigorously excluded by the fact that each stereoisomer maintains its identity under all the changes of physical condition that could be applied. Although there is always a considerable difference in solubility, one stereoisomer could never be converted into another (*e. g.*, the less soluble modification) by means of a solvent. Fusion and subsequent solidification, in contact with its own crystals or even with the solid phase of the other form, never produced any transformation of one stereoisomer into the other. A mixture of the two forms always has a very much lower melting point than either pure form (there is a lowering sometimes of from 20° to 50°) and this low-melting mixture,

[1] *Loc. cit.*

allowed to solidify, gives the same melting point when heated again, showing that there is no change of form even under these, the most favorable conditions for the transformation of crystal modifications. Dr. Hilpert was also able to prove the persistence of the configuration and structure of the molecules of the stereoisomeric methyl chlorimido-*p*-nitrobenzoates in the gas form by distilling them at 134° under 1 mm. pressure.

IV. The Transformation, Chemically, of the Less Stable Stereoisomer into the More Stable One, and Vice Versa—a Reversible Reaction.

Reagents which are easily absorbed by unsaturated bodies, the halogens and the halogen acids, and easily given off again, have often been observed, sometimes when present only in traces, to have the power of transforming one form of the cis-trans stereoisomers of the ethylene series[1] into the other form, and the halogen acids have also been found to effect a similar transformation when acting on stereoisomeric oximes.[2] The change is supposed to be due to the addition of the reagent to the double bond causing the stereoisomerism, although the addition, at least in some cases, is not complete.[3]

For stereoisomeric chlorimidoesters it was thought that a similar transformation, especially of the less stable into the more stable form, should be effected by chlorine. Without destroying or otherwise affecting the compounds, chlorine could form unstable addition products, which, by the loss of chlorine after the opening of the double bond and a rotation of the now singly bound carbon atom, could form the other stereoisomer:

$$\begin{matrix} R{-}C{-}OR' \\ \| \\ Cl{-}N \end{matrix} + Cl_2 \rightleftarrows \begin{matrix} R{-}C^{OR'}_{Cl} \\ | \\ Cl{-}N{-}Cl \end{matrix} \rightleftarrows \begin{matrix} R{-}C{-}OR' \\ \| \\ N{-}Cl \end{matrix} + Cl_2.$$

A consideration of such an action leads to the conclusion that if it takes place at all it must be reversible to a certain

[1] See Meyer and Jacobson: Organische Chemie, Vol. II, p. 685.
[2] *Ibid.*, 509.
[3] *Ibid.*, 686.

extent, producing a condition of equilibrium, since chlorine could be added and lost in either way.

Both these suppositions have been confirmed by experiment. The change of one stereoisomer into its more stable mate was first carried out with α-methyl chlorimido-*m*-nitrobenzoate, which is converted into the more stable β form by the action, for two minutes,[1] of dry chlorine at 90°. For the ethyl ester it was found that the β compound is converted into the α compound, which, in this case, is the more stable one.[2] Hilpert[3] not only used this method successfully on the stereoisomers he discovered but he also proved in the two cases tried (the α and β forms of methyl chlorimido-*m*-nitrobenzoate and the two forms of the same ester of *p*-nitrobenzoic acid) that the action is really a reversible one, the more stable form going in each case to a slight extent over into the less stable modification, which was isolated in sufficient quantity to permit of its complete identification.

Hilpert[3] has also found a second means for effecting such a reversible transformation in the boiling of the stereoisomeric methyl chlorimidonaphthoates with water; probably a trace of hypochlorous acid is formed and acts as represented for chlorine in the above equations.

In these transformations, fulfilling every anticipation based on the well-known behavior of stereoisomers of this type, we have, therefore, a final confirmation of the conclusion that the relations of the isomers we are dealing with are those of stereoisomers.

V. The Configurations of the Stereoisomeric Chlorimidoesters.

Little direct evidence as to which configuration belongs in each instance to the stereoisomers distinguished as α and β can be brought. Towards heat (200°), effecting, by destructive distillation, partly a "Beckmann rearrangement,"[4] partly a decomposition into nitriles, no difference in the behavior of the two stereoisomers of a pair could be detected, either

[1] This was carried out with Mr. Hale; *vide* a later report.
[2] *Ibid.*
[3] *Loc. cit.*
[4] *Vide* the later report with Hale and Eckstein.

qualitatively or quantitatively. The best evidence we have on the question of configuration is based on the relative stability of the methyl and ethyl esters, as discussed in Dr. Hilpert's report, and as the subject is not of very great moment for the argument of this paper, it will be sufficient to refer here to my young collaborator's paper for the discussion of the question.

VI. The Stereoisomeric Chlorimidoesters and the "Syn" and "Anti" Stereoisomerism of Nitrogen Derivatives.

The theory of Hantzsch and Werner[1] that the stereoisomerism of nitrogen derivatives containing a doubly bound nitrogen atom is of the same nature as the stereoisomerism of ethylene derivatives containing doubly bound carbon atoms has given a satisfactory and uniform basis of explanation of all the observed cases of nitrogen stereoisomers. According to their view we have the two configurations,

$$\begin{matrix} X-C-Y \\ \| \\ Z-N \end{matrix} \quad \text{and} \quad \begin{matrix} X-C-Y \\ \| \\ N-Z \end{matrix} .$$

As is well-known, when the theory was first advanced, Victor Meyer,[2] the discoverer of the first proved cases of nitrogen stereoisomerism, the benziloximes and dioximes, at first opposed Hantzsch's theory and thought it possible that the difference in configuration might be due to peculiarities of the hydroxylamine molecule; and Hantzsch himself said at the time:[3] "In spite of all the facts being in favor then of the first configurations"—(Hantzsch's, as given above)—"they do not, also according to our own opinion, contain the definite proof of the theory. This proof would only be brought when the behavior of hydroxylamine should no longer be found exceptional and cases of stereoisomerism for other nitrogen derivatives of the general form XYC:NZ than the oximes should be discovered." The discovery by Hantzsch, then, of the stereoisomeric phenylhydrazones brought the evidence that hydroxylamine was not unique among nitrogen compounds

[1] Ber. d. chem. Ges., **23**, 11, 1243 (1890).
[2] *Ibid.*, **16**, 503 (1883), etc.
[3] *Ibid.*, **24**, 3515 (1891).

in producing stereoisomers, and Hantzsch and Werner's theory has secured a well-merited general acceptance and has proved its usefulness, particularly also in the case of diazo derivatives.

Nevertheless, it has remained a fact, as far as we can discover,[1] that all efforts to produce unquestioned stereoisomers of the above type from amine derivatives other than hydroxylamine and hydrazine, in which Z (in the above structure) is a simple radical, such as phenyl or carbethoxyl, etc., have remained hitherto without result, even in the extended investigations carried out, up to a recent date, under the direction of the creator of the above theory.[2] In the few cases we have found in the literature, in which, for instance, stereoisomeric aniline derivatives were supposed to have been obtained, structural isomerism, especially, and physical isomerism and polymerism have not been rigorously excluded,[3] so that these compounds have never been accepted as unquestioned representatives of stereoisomerism among nitrogen derivatives. On the other hand, the decided chemical similarity between hydroxylamine and hydrazine has made it desirable to discover stereoisomers in no wise connected with the oxime and hydrazone class of compounds. To this fact, the search for derivatives in which Z would be some simple carbon radical has been largely due.

The newly discovered stereoisomeric chlorimidoesters, therefore, fill, we believe, a long felt gap in the experimental development of Hantzsch and Werner's theory. In this case, Z assumes the simplest possible form—a single chlorine atom—and a proof of stereoisomerism, excluding structural isomerism, polymerism, and physical isomerism, has been possible by rigorous methods of organic and physical chemistry.[4]

[1] See, for instance, Hantzsch: Stereochemie (1904), p. 141; Ber. d. chem. Ges., **34,** 822 (1901).

[2] Ber. d. chem. Ges., **24,** 3518 (1891); **26,** 9 (1893); **26,** 926 (1893); **28,** 977 (1895); **30,** 3003 (1897); **34,** 822 (1901).

[3] *Vide* Meyer and Jacobson's criticism: Organische Chemie, II, p. 509; and Hantzsch's: Ber. d. chem. Ges., **34,** 822 (1901); and Hantzsch's Stereochemie (1904), p. 141. Also, Meyer and Jacobson's Organische Chemie, 2d Edition, I, p. 785 (1906).

[4] The work on this type of stereoisomers is being continued. Mr. Raiford is trying to obtain stereoisomeric quinonechlorimides and Mr. Rosario del Valdeczo is working on the possibility of isolating stereoisomeric imidoesters. Mr. Peterson is working on stereoisomeric chlorimidoketones and we have evidence of the existence of two chlorimido-*p*-chlorbenzophenones.

Their existence is in complete agreement with Hantzsch and Werner's fundamental hypothesis.

CHICAGO, September, 1907.

INVESTIGATION OF THE CLAISEN CONDENSATION. II. A CONTRIBUTION TOWARDS THE ELUCIDATION OF THE MECHANISM OF THE REACTION.

BY J. BISHOP TINGLE AND ERNEST E. GORSLINE.

THEORETICAL.

The Effect on the Reaction of Varying Conditions.

In our previous paper on this subject[1] we have presented evidence which proves that ether, pyridine, and quinoline act as catalytic agents in promoting the Claisen condensation between certain ketones and esters, in the presence of sodium. The present communication describes a considerable number of experiments which we have carried out for the purpose of determining the influence on the reaction and, therefore, on the yield of diketone of changes in the conditions. That such changes may exert a marked influence was shown some years ago by J. Bishop Tingle[2] in the case of camphoroxalic acid. We have studied the effect of variation of the temperature and of the solvent, and also the result of employing, as condensing agents, such substances as sodium, sodamide, and calcium. We have also carried out a few experiments with sodium ethylate free from alcohol and with sodium ethylate in absolute alcoholic solution. The last two reagents named have been used frequently by Claisen[3] and many other chemists, and the employment of metallic sodium is, of course, quite common. It is believed that the use of metallic calcium in this connection is new.

A. The Use of Calcium and Sodamide as Condensing Agents.—Camphor and the ethyl esters of oxalic, benzoic, and cinnamic acids have been condensed, using calcium and sodamide

[1] THIS JOURNAL, **37**, 483 (1907).
[2] *Ibid.*, **19**, 393 (1897).
[3] Ber. d. chem. Ges., **38**, 709.

as the condensing agents. The temperature and solvent employed were also varied in each case. The results show that with camphor as the ketone, metallic calcium and sodamide are practically useless as condensing agents unless alcohol is added to the materials employed. Even then, the reaction must be carried out at a relatively high temperature. Under these conditions a fair yield may be obtained. This is quite different from the results recorded by Claisen,[1] who worked with sodamide, using acetone and acetophenone with ethyl acetate, and acetone with ethyl benzoate. It furnishes an illustration of the weighty influence exercised on the reaction by the nature of the ketone or aldehyde, and also by that of the ester.

Another matter of some importance and interest which this part of the work has demonstrated concerns the nature of the "solvent product" (*vide* p. 60). In the case of condensations between camphor and ethyl oxalate, in the presence of sodium, considerable quantities of camphoroxalic acid can be extracted from it.[2] The same is true when sodamide is used as the condensing agent, and also when this substance or sodium is brought into reaction with camphor and ethyl cinnamate. The results with calcium are in sharp contrast with this. In no single case has a trace of the condensation product been detected in the "solvent product." The difference may, of course, be due to the different solubilities of certain sodium or calcium compounds formed during the reaction.

B. The Effect of Sodium Ethylate upon the Condensation.—The addition of a mere trace of alcohol, or of a solution of sodium ethylate in absolute alcohol, to the mixture of ketone, ester, sodium, and solvent starts a reaction very quickly, but the yield of the diketone is always greatly reduced. The important bearing of this fact upon one of the theories concerning the mechanism of the reaction will be discussed later.

C. The Effect of Various Solvents and Temperatures.—This factor has already been discussed in our previous communication.[3] Some additional experiments have been performed

[1] Ber. d. chem. Ges., **38**, 695 (1905).
[2] J. Bishop Tingle: THIS JOURNAL, **19**, 393 (1897).
[3] THIS JOURNAL, **37**, 483 (1907).

which confirm the conclusion that practically no difference is made in the final result by the use of any one of the following solvents: petroleum ether (b. p. 36°), ligroin (b. p. 50°–55°), hexane (b. p. 90°), benzene, toluene, xylene. As a rule the condensation proceeds more slowly in these media than it does in ethereal solution. In the case of some esters or ketones, however, the tendency to react is so great that variation of the solvent is without apparent effect on the velocity of the reaction or on the yield of diketone produced.

The effect of changing the temperature was also dealt with in our previous paper,[1] and some additional experiments confirm the results obtained. In general, under similar conditions, the influence of the factors temperature and time are, roughly, inversely proportional. Moreover, better yields of diketone are obtained with higher- than with lower-boiling solvents, provided, of course, the temperature is not sufficiently great to decompose the products of the reaction.

D. The Influence of the Constitution of the Ester upon the Condensation.—On account of a delay in receiving a shipment of materials the work in this connection is much less complete than could be wished. The compounds employed may be classified as follows:

A. Aliphatic Series: Esters of formic, acetic, butyric, oxalic, malonic, and succinic acids.

B. Aromatic Series: Esters of benzoic, nitrobenzoic, cinnamic, and phthalic acids.

To obtain the condensation products when the above esters are allowed to react with camphor, it is generally necessary to extract with ether the acidified aqueous solution obtained by pouring the condensation product into ice water and removing the solvent layer. In a few cases the product will precipitate upon acidulation. Claisen[2] obtained oxymethylenecamphor in this way and the product of the ethyl phthalate-camphor condensation precipitates upon acidulation. By extracting with ether, every product, including the two above mentioned, is obtained in the form of a heavy, reddish brown

[1] *Loc. cit.*

[2] Bishop, Claisen, and Sinclair: Ann. Chem. (Liebig), **281**, 328.

oil. J Bishop Tingle[1] obtained camphoroxalic acid by the hydrolysis of the oil obtained by condensing camphor and ethyl oxalate. By the hydrolysis of the ether extract of the ethyl formate-camphor condensation Claisen's oxymethylene-camphor can be obtained. During this investigation compounds analogous to these have been isolated from the condensation of camphor with ethyl benzoate and with ethyl phthalate. No attempt has been made to purify the products obtained from the condensation of all of the above-named esters with camphor, this being beyond the scope of this investigation. It seems practically certain, from the results which have been accumulated, that these products are compounds similar in nature to camphoroxalic acid and oxymethylenecamphor. Enough work has been done, however, to show that their preparation in large quantities and in a pure form presents serious difficulties.

The experimental evidence shows that the reaction is markedly influenced by the nature of the ketone or aldehyde employed, and also by that of the ester. There is reason to doubt whether this influence is confined to a variation in the velocity. In some cases, at least, it seems to extend to the actual mechanism of the reaction. An effort has been made to obtain light on this point by a systematic study of the effect produced by variation in the constitution of the ester.

Until more work has been done on this subject it would be premature to generalize. It appears, however, that the readiness with which the reaction takes place is increased by the proximity of two carbethoxy groups. There is some evidence, which will be presented later, indicating the possibility that the mechanism of the reactions resulting in the formation of diketones is different in the case of the aliphatic and the aromatic esters.

E. The Catalytic Effect of Ether and the Tertiary Bases in the Claisen Condensation, and also in the Formation of the Grignard Reagent.—In a previous paper[2] we were able to show that ether acts as a powerful catalytic agent in promoting

[1] Inaug. Diss., Munich, 1889.
[2] *Loc. cit.*

the Claisen condensation, and that this property is shared by pyridine and quinoline. There is, thus, a complete analogy between the Claisen and the Grignard reactions.

A similar catalytic action of ether has been observed in one or two other cases. Prof. A. Michael has been good enough to point out to us that Menschutkin[1] was probably the first to show that the addition of ethyl iodide to trimethylamine takes place 200 times faster in ether than in ligroin. Freer,[2] from his experiments with sodium and acetone, which do not react except in the presence of a solvent of the latter, concludes that "ether is not an indifferent solvent."

F. The Action of Ether and the Tertiary Bases on the Acetoacetic Ester Synthesis.—As is well known, ethyl acetoacetate is formed by condensing two molecules of ethyl acetate with one atom of sodium, using an excess of the ester as the solvent. The statement has been made by Higley[3] that in the presence of a solvent there is no trace of acetoacetic ester formed. Bacon,[4] on the other hand, whose results Higley claims to have confirmed, admits that traces of acetoacetic ester were obtained when ten parts of ether were used as a solvent.

In an interesting series of papers by Bouveault and Locquin,[5] evidence is presented to show that, while ethyl acetoacetate is formed by the condensation of ethyl acetate and sodium when an excess of the ester is used as a solvent, when dissolved in benzene or ether the reaction results in the formation of the compound $CH_3COCH(OH)CH_3$, after treating the product of the reaction with water. Similar compounds were also obtained by condensing esters of the higher aliphatic acids with sodium.

We have carried out some experiments on the acetoacetic ester condensation, using as solvents small quantities of ether, petroleum ether (b. p. 36°), and pyridine. The catalytic effect of ether and pyridine on the velocity of the reaction is appar-

[1] J. Chem. Soc., **54**, 901 (1888); Z. physik. Chem., **6**, 41 (1890).
[2] This Journal, **15**, 582 (1893); Bacon and Freer: *Ibid.*, **38**, 367 (1907).
[3] This Journal, **37**, 293.
[4] *Ibid.*, **33**, 77–80.
[5] Bull. Soc. Chim. **36**, 629.

ent. Moreover, when purifying the product in the manner described by Gattermann,[1] there is obtained in each case a small amount of liquid which boils at 175° to 177° and gives an intense coloration with ferric chloride. The statement that no acetoacetic ester is formed in the presence of a solvent would seem to require verification. Furthermore, a long series of experiments fails to show that ether or the tertiary bases have any catalytic action when sodium reacts with esters to form compounds of the class $\begin{matrix} C_6H_5CONa \\ \| \\ C_6H_5CONa \end{matrix}$. This would necessarily be the case here if only a compound of the above nature was formed.

It seems probable that the two reactions take place simultaneously, and that in the presence of solvents the reaction $2CH_3COOC_2H_5 + 4Na \rightarrow \begin{matrix} CH_3CONa \\ \| \\ CH_3CONa \end{matrix} + 2NaOC_2H_5$ is by far the preponderating one.

G. The Mechanism of the Reaction.—The Claisen condensation is explained by its discoverer as follows:[2] When camphor and ethyl formate are condensed by means of sodium wire, sodium borneolate and sodium camphor, $C_8H_{14}\begin{matrix} CH \\ \| \\ CONa \end{matrix}$, are first formed, and the latter, with the ester, yields the ortho compound, $HC\begin{matrix} ONa \\ -OC_{10}H_{15} \\ OC_2H_5 \end{matrix}$. This hypothetical intermediate product then reacts with camphor:

$$HC\begin{matrix} ONa \\ -OC_{10}H_{15} \\ OC_2H_5 \end{matrix} + \begin{matrix} H \\ H \end{matrix}\!>\!C\!<\!\begin{matrix} \\ \\ OC \end{matrix}\!>\!C_8H_{14} \rightarrow C_8H_{14}\begin{matrix} C:CHONa \\ | \quad H \\ CO \end{matrix} + C_{10}H_{16}O + C_2H_5OH.$$

He explains similarly the acetoacetic ester synthesis, which is a special case of the Claisen condensation:

[1] Prac. Meth. Org. Chem., 2nd Am. Ed., p. 155.
[2] Ann. Chem. (Liebig), **281**, 328.

$$CH_3COOC_2H_5 + NaOC_2H_5 \rightarrow$$

$$CH_3C(ONa)(OC_2H_5)_2 + H_3CCOOC_2H_5 \rightarrow$$

$$CH_3C(ONa):CHCOOC_2H_5 + 2C_2H_5OH.$$

As seen from the above reactions, sodium ethylate is the active condensing agent. In the case of the acetoacetic ester synthesis a trace of alcohol is regarded as necessary to start the reaction. This reaction is cumulative because an increased amount of alcohol is being formed, and this, being acted upon by the sodium, gives an increasing amount of the active condensing agent—sodium ethylate. However, Claisen himself finds that sodium is a better condensing agent than sodium ethylate in alcoholic solution or sodium ethylate free from alcohol.

The explanation of the acetoacetic ester synthesis now advanced by Nef[1] is very similar to that of Claisen. The alcohol present in the ester forms sodium ethylate, and this reacts with ethyl acetate to form the intermediate compound of Claisen, $H_3CC(ONa)(OC_2H_5)_2$. This substance is then supposed to dissociate, giving $CH_3C(ONa)(OC_2H_5)$ | | $+ C_2H_5OH$.

Another molecule of ester is assumed now to be added:

$$CH_3C(ONa)(OC_2H_5) \text{ | | } H\ CH_2COOC_2H_5 \rightarrow CH_3C(ONa):CHCOOC_2H_5 + C_2H_5OH.$$

Higley[2] suggests that when ethyl acetate is treated with sodium two independent reactions take place simultaneously:

$$\text{I.}\quad 2CH_3COOC_2H_5 + 4Na \rightarrow \begin{matrix} CH_3CONa \\ \| \\ CH_3CONa \end{matrix} + 2NaOC_2H_5.$$

[1] Higley: THIS JOURNAL, **37**, 293.
[2] *Ibid.*

II. The sodium ethylate formed in (I.) reacts on the ethyl acetate as follows:

$$\text{II.}\quad CH_3COOC_2H_5 + NaOC_2H_5 \rightarrow CH_4C(ONa):CHCOOC_2H_5 + 2C_2H_5OH.$$

Here, again, it will be noted that sodium ethylate is the active condensing agent.

Higley concludes that this synthesis ought to give the best results when sodium ethylate is used as the condensing agent, as the reaction would then proceed entirely in the direction of the formation of acetoacetic ester until the point of equilibrium is reached, the reaction being a reversible one. This, he states, is reached when about 36.5 per cent of the acetoacetic ester has been formed. As found experimentally, however, the yield of the ester is not improved by the use of sodium ethylate, and, on the other hand, it is probable that sodium wire is the better condensing agent. This fact has been recorded by Claisen[1] and others, and the experiments herein described lead to the same conclusion.

Unless the superiority of sodium ethylate can be proved, the explanation of Higley is certainly not a logical one. Taking into consideration the present evidence as to the yield obtained in this synthesis when sodium and sodium ethylate are employed, if his explanation were correct, we should have the phenomenon of a condensing agent, formed at the expense of some of the ester used, proving more efficient than does the same agent when it is added to the original amount of the ester.

If the hypothesis of Claisen is correct, it is evident that sodium ethylate itself ought to be an excellent accelerator. This is found to be the case. In a series of experiments with camphor and the esters of various acids, using petroleum ether (b. p. 36°) as a solvent, the addition of a little alcoholic sodium ethylate accelerated a reaction to a marked degree. Absolute alcohol proved to be a still stronger accelerating agent. On the other hand, the use of sodium ethylate free from alcohol affected very little, if at all, the speed of the reaction.

[1] Ber. d. chem. Ges., **38**, 709.

The most striking fact brought out by these experiments is the *great reduction in the yield of the diketone, when alcohol or alcoholic sodium ethylate is added to the reacting materials.* In the condensation of ethyl phthalate and camphor, the addition of two drops of alcoholic sodium ethylate reduced the yield of diketone about 50 per cent. The addition of a little alcohol causes an equally great reduction. A similar reduction was observed in every case where either of these reagents was used. When alcohol is employed it undoubtedly attacks some of the sodium, but this in no way accounts for the great reduction in the yield of the product; the solution of sodium in alcohol which was employed in our experiments had been treated with sodium until no more would dissolve.

Sodium ethylate free from alcohol did not materially decrease the yield of the diketone, but it is not as good a condensing agent as sodium wire. Claisen,[1] in his paper on oxymethylenecamphor, states that alcoholic sodium ethylate is the weakest condensing agent, being followed in this respect by sodium ethylate free from alcohol and by sodium wire, in the order named. It has been experimentally established during this work that there is no difference in the solubility of sodium ethylate in ether, which was the solvent generally used by Claisen, and in the other solvents here employed. This is true of both the alcoholic solution of sodium ethylate and of that reagent free from alcohol.

Michael and others have pointed out that one of the weakest points in Claisen's explanation of the reaction which bears his name consists in the way in which he explains the influence exerted by sodium ethylate on the nature and extent of the changes involved. If sodium ethylate, or an analogous compound, is the active agent in promoting the condensation, then the addition of this compound should facilitate the reaction in question instead of retarding it. If the condensation is a reversible reaction this view would apply still more strongly. With regard to Claisen's claim that a trace of alcohol is necessary to start the reaction, we have already pointed out that two drops of alcoholic sodium ethylate reduces the yield by

[1] *Loc. cit.*

nearly one-half, and that alcohol has a similar effect. It is hard to understand how it can reasonably be claimed that a reaction depends on the presence of a hypothetical trace of alcohol, when, as a matter of fact, the yield is so greatly reduced by the presence of the smallest tangible amount of the substance. The attempted explanation by Claisen[1] and by Higley[2] of the superior condensing power of sodium is, to say the least, not satisfactory.

A number of experiments have been carried out with the following objects in view: (*a*) To determine the effect of varying the amount of sodium used in the condensation. (*b*) To find out at what point in the condensation the catalytic agent exerts its accelerating influence. (*c*) To determine whether there is a difference in the mechanism of this reaction when aromatic esters are used instead of those of the aliphatic group.

Bouveault and Locquin[3] showed that when sodium acts upon the aliphatic esters in the presence of a solvent the reaction proceeds as follows:

$$\begin{matrix} RCOOC_2H_5 \\ | \\ RCOOC_2H_5 \end{matrix} + 4Na \rightarrow \begin{matrix} RCONa \\ \| \\ CCONa \end{matrix} + 2NaOC_2H_5.$$

The experiments with ethyl oxalate, herein described, show that this similarly combines with four atoms of sodium to one molecule of the ester. In the case of ethyl malonate, only two atoms of sodium will react with each molecule of the ester, and the first atom of the metal causes a generation of hydrogen while the second does not. In view of the reactions of the other esters of the aliphatic group, it is difficult to reconcile this reaction with the formula usually assigned to ethyl malonate. On the other hand, it has been suggested by various chemists that in some reactions its behavior accords better with the formula $C_2H_5OC(OH):CHCOOC_2H_5$.[4] If this hypothesis is correct we should expect that the first atomic proportion of sodium would liberate hydrogen from the hydroxyl group, and that the resulting compound, $C_2H_5OC(ONa):CHCOOC_2H_5$, would form,

[1] Ber. d. chem. Ges., **38,** 712.
[2] *Loc. cit.*
[3] *Ibid.*
[4] Cf. D. Vorlander: Ber. d. chem. Ges., **36,** 268 (1903); E. Fischer and Dilthey: *Ibid.*, **35,** 844 (1902); Hans Meyer: *Ibid.*, **39,** 198 (1906).

with another portion of the metal, sodium ethylate and a substance having the constitution $\begin{matrix} C_2H_5OC(ONa):CHCONa \\ \| \\ C_2H_5OC(ONa):CHCONa \end{matrix}$. In the formation of camphoroxalic acid, J. Bishop Tingle[1] found that the best yield resulted from the use of one atom of sodium and 1.5 molecules of camphor to one molecule of the ester, using ligroin as a solvent. Wislicenus[2] has also studied the effect of an excess of sodium on ethyl acetate.

The experiments which have been performed in this investigation have brought out the following facts: When the esters of the aliphatic series are condensed with camphor, the use of more than one atomic proportion of sodium does not increase the yield of the diketone. The catalytic agent does not accelerate the reaction between sodium and the ester, nor between sodium and camphor. Sodium camphor is a weak condensing agent. Only traces of the acid involved are found in the products of the condensation.

When ethyl benzoate and camphor are condensed, two atoms of sodium combine with one molecule of the ester to give the compound $\begin{matrix} C_6H_5CONa \\ \| \\ C_6H_5CONa \end{matrix}$, which is the product obtained by Nef[3] upon treating benzil with sodium, and is analogous to the compound obtained by Bouveault and Locquin[4] with the aliphatic esters. When this compound is treated with water, sodium benzoate and benzyl alcohol are formed in equimolecular proportions. Under suitable conditions, however, the hypothetical product of hydrolysis, $\begin{matrix} C_6H_5COH \\ \| \\ C_6H_5COH \end{matrix}$, changes into benzoin, $C_6H_5CH(OH)COC_6H_5$; and this has been isolated in the form of its *m*-nitrobenzene derivative. The best yield of diketone is obtained when two atoms of sodium are allowed to react upon the ester, and sodium camphor is then added. When camphor was mixed with the reaction products of the ester with two atoms

[1] J. Chem. Soc., **57**, 652.
[2] Ann Chem. (Liebig), **186**, 163.
[3] *Ibid.*, **308**, 287.
[4] *Loc. cit.*

of sodium, the yield of the diketone was less than when the ester, camphor, and two atoms of sodium were allowed to react together.

The products obtained from the ethyl benzoate-camphor condensation are benzoic acid, benzyl alcohol, and the diketone. Apparently the formation of the diketone diminishes the amount of the benzyl alcohol obtained but does not effect the quantity of benzoic acid formed. It was found that only traces of benzoic acid are produced from the hydrolysis of ethyl benzoate during the process used for the extraction of the diketone, so that the presence of the acid in the condensation product cannot be accounted for in this way. In the condensation of ethyl cinnamate and camphor a large quantity of the acid is also obtained in the product. In the condensation of ethyl phthalate, however, only traces of the acid are found.

These results seem to show that the mechanism of the reaction is not always the same. Nevertheless, the relative strength of the condensing materials employed, the effect of catalytic agents, and the influence of sodium ethylate and alcohol seem to extend to the condensation of esters of both the aliphatic and aromatic series.

It has been pointed out that the experimental facts obtained in this investigation cannot be reconciled with the theories of Claisen, Nef, and Higley concerning the mechanism of the reaction. An alternative theory, which was advanced by A. Michael,[1] may be expressed as follows: Sodium at first acts upon one molecule of ethyl acetate, displacing hydrogen,

$$CH_3COOC_2H_5 + Na \longrightarrow CH_2NaCOOC_2H_5 + H.$$

This substance then reacts upon a second molecule of the ester, giving the product $CH_3C(ONa)(OC_2H_5)CH_2COOC_2H_5$. Alcohol is now eliminated with formation of the product $CH_3C(ONa):CHCOOC_2H_5$. When sodium ethylate is used as a condensing agent, it is assumed that it causes, by the loss of some of its energy, an aldol condensation, forming, for example,

[1] Ber. d. chem. Ges., **33**, 3731; **38**, 1934.

the product $CH_3C(OH)(OC_2H_5)CH_2COOC_2H_5$. This then yields the ortho sodium derivatives formulated above, and finally, by the loss of alcohol, ethyl sodioacetoacetate. Michael, later, adopted the view that the compound formed when sodium acts on ethyl acetate is $CH_2:C(ONa)OC_2H_5$ instead of $CH_2NaCOOC_2H_5$. In view of recent work on tautomerism it seems likely that these two forms are in equilibrium.

The most striking differences between the two hypotheses appear to be the following: (1) Claisen assumes that it is not sodium itself which is the active agent, but a compound of the metal, such as sodium ethylate or sodium camphor; (2) The intermediate ortho compound is supposed by him to be an O- and not a C-derivative.

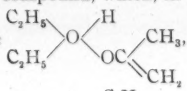
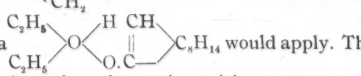
The reversal of the ethyl acetoacetate condensation, under the influence of sodium ethylate, has been studied very successfully by W. Dieckmann.[1] He shows that the velocity of the decomposition depends upon the degree of acidity of the particular β-ketonic ester employed. In conjunction with A. Kron,[2] in a paper which appeared while this article was in the press, he has also proved that the condensation may take place between esters and ketones of the type HCR_2CO. This fact is accounted for without difficulty by Michael's explanation of the acetoacetic ester condensation, but is incompatible with Claisen's theory. According to the latter the formation of the hypothetical intermediate compounds requires two atoms of hydrogen from the ketone, consequently the condensation can occur only between esters and ketones which contain the group H_3CCO or H_2CRCO.

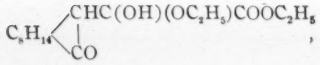
With two reservations, noted below, the explanation of the mechanism of the condensation offered by Michael seems to be entirely satisfactory. The first reservation concerns the reaction of sodium on esters. Bouveault and his colleagues have proved how generally this reaction applies to compounds of the aliphatic series with the exception of ethyl acetate, which, as

[1] Ber. d. chem. Ges., **33**, 2670 (1900).
[2] *Ibid.*, **41**, 1260 (1908).

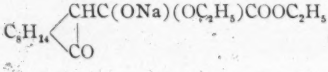
they have noted, acts in a different manner. It has been shown in the preceding pages that the reaction is the chief one which occurs with sodium and ethyl benzoate, in the presence of camphor; indeed, there can be no doubt that this, and not the Claisen condensation, is the preponderating reaction under the conditions described. It occurs, probably, in all cases where esters and sodium are brought together, its extent being determined by the nature of the ester and the experimental conditions. Obviously, these remarks, which are merely made for completeness, in no way modify Michael's explanation of the Claisen reaction itself.

The second point to which attention must be called is the catalytic effect of ether and the tertiary bases. In considering this the following facts must be remembered: (1) The substances in question accelerate the Claisen condensation; (2) they act in the same manner in connection with the formation of the Grignard reagent (Grignard, Tschelinzeff); (3) ether facilitates the addition of ethyl iodide to triethylamine (Menschutkin); ether is markedly active in promoting the action of sodium on acetone (Freer); ether, as compared with petroleum ether, facilitates the action of sodium on ethyl acetate; ether is without effect on the interaction of sodium and ethyl benzoate.

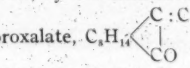
The explanation already offered of the effect of ether and the tertiary bases on the formation of the Grignard reagent can be applied, *mutatis mutandis*, to cover, in a satisfactory manner, the points mentioned above. It postulates the formation of an oxonium compound, which, in the case of acetone, for example, would be  , whereas, with a ketone such as camphor the formula  would apply. The next step in the condensation of camphor with an ester, such as ethyl oxalate, for instance, would be, adopting Michael's formulation, the production of the compound



followed by that of the sodium derivative,



which then, by the elimination of alcohol, gives ethyl sodiocamphoroxalate,



The above oxonium derivatives might also be expected to be more reactive with sodium than compounds having the ordinary ketone structure. The essential point in the explanation which is offered is that it represents a change into a secondary form of the ketone.

Experimental.

Method of Experimentation.—Unless otherwise stated, the ketone and ester were dissolved in the solvent employed and the sodium was cut under another portion of the solvent and quickly transferred to the press. The wire was now rapidly forced into the flask containing the solution, the flask being then attached to a reversed condenser.

The product of the reaction was poured into ice water, the mixture well shaken, and the lighter layer removed and dried over calcium chloride. Then the solvent was distilled away. The material remaining after the distillation will be referred to in the following pages as the "solvent product." The aqueous solution obtained after the separation of the solvent was, in some cases, extracted with ether; but except in a few special instances this treatment was found to be without appreciable effect, and the practice was discontinued. The aqueous solution was next acidified and extracted four times with ether. The ethereal solution, after being dried over calcium chloride, was distilled. The residue which had been dissolved in the ethereal solution will be referred to as the "acidification product."

For the acidification, acetic, dilute hydrochloric, or dilute sulphuric acid was employed. Carbon dioxide was also used. No difference in the effect of these substances has been discovered, and consequently, in the later stages of the work, dilute hydrochloric acid was used. A number of chemists have employed acetic acid for the preparation of such compounds as we have investigated; the mineral acid is far more convenient, and contamination of the "acidification product" with the excess of acetic acid extracted by the ether is avoided.

During the removal of the organic solvents by distillation the temperature was never allowed to rise above 100°, and was usually below this point. If necessary, the pressure was reduced.

A portion of the product of the reaction was dissolved in a few drops of ordinary alcohol (95 per cent). If alkali was present, the liquid was made faintly acid with pure, dilute hydrochloric acid. A few drops of an alcoholic solution of ferric chloride were added. The production of a reddish purple coloration was accepted as evidence of the formation of the enolic modification of the diketone.

The yields are sometimes referred to as "fair," "good," "poor," etc. It is a matter of regret that it has not been possible to be more definite on this point. Of course, the crude products of the reaction could have been weighed, and, in some cases, they were; but the figures obtained in this way would have been but little more definite and would probably have proved somewhat misleading. Reliable results can only be obtained by working out a method of purification for each individual compound, and it was impossible to attempt this because of the time required. The object has been to obtain general information and data, which could be used in a closer and more intensive study of these separate substances individually.

Preparation of Solvents and Reagents.—The solvents which have been employed were dried by means of sodium wire. When this was no longer tarnished, the liquid was decanted or filtered into a separate vessel, and a fresh portion of sodium wire was added. The solvent was allowed to remain in contact with this until used.

The esters were generally distilled, or their boiling points or melting points taken. Any free acid or acid ester was removed by washing with aqueous sodium hydroxide, and the compound was then dried by prolonged contact with calcium chloride.

The sodamide which was employed was made by the admirable method described by Winter,[1] which he worked out under the direction of Prof. Renouf.

The metallic calcium was the commercial article, prepared electrolytically. This was turned to thin shavings on a lathe, the outer portion covered with oxide being discarded. The shavings were washed in dry ether, rapidly dried in warm air, and placed in a warm, dry bottle which was then sealed with paraffin. Under these conditions it remained bright for an indefinite time. The statement has been made[2] that the oxide adhering to the original sticks of the metal can be removed by immersion for a short time in 70 per cent alcohol. This plan was tried but the results were not encouraging.

The solution of sodium ethylate in alcohol was made by adding clean, bright sodium to absolute alcohol, suitably protected from moisture, until no more would dissolve.

Sodium ethylate free from alcohol was prepared by dissolving the sodium in a mixture of absolute alcohol and petroleum ether, the liquid being finally boiled for two hours to complete the reaction. It was now distilled until the contents of the flask were dry. The residue was quickly powdered and sifted, and used for further reactions as soon as possible after it was prepared.

The absolute alcohol was obtained by treating ordinary alcohol first with quicklime, then with dehydrated copper sulphate, and finally boiling it for several days with calcium turnings, from which it was eventually distilled. It was well protected from moisture and was used soon after its preparation.

The apparatus in which the condensation was carried out was carefully washed with alcohol and ether and dried by a current of hot air. During the whole course of the experiment the vessels in use were protected from moisture by means of

[1] J. Am. Chem. Soc., **26**, 1484 (1904).
[2] Ber. d. chem. Ges., **38**, 3613 (1905).

calcium chloride tubes. Comparative experiments show that with some substances, at any rate, this latter precaution is unnecessary. It was adopted, however, in the case of all experiments which are described, unless otherwise stated expressly. It seems certain that the presence of traces of moisture is practically without effect on the condensation of some substances.

The sodium wire was obtained by placing clean, bright sodium in a sodium press and forcing it directly into the flask and solvent to be used for the condensation.

For the sake of brevity the work described in the following pages is given as if it were the result of single experiments. Actually, however, each experiment has been performed twice, and in many cases three or more times, until the evidence concerning the constancy and correctness of the observations made was satisfactory. Numerous changes were made in what may be termed the minor experimental conditions, but it has not been considered necessary to record these unless their results established some point which seems to be of importance.

Experiments Showing the Effect of Different Condensing Agents.

A. Experiments with Calcium Turnings.

Experiment 1.—22.8 grams camphor (1.5 mols.); 14.6 grams ethyl oxalate (1 mol.); 4.0 grams calcium (1 mol.); 400 cc. hexane (b. p. 90°).

After boiling for 40 minutes no signs of a reaction were observed. The addition of 25 cc. of absolute alcohol produced no effect. The solvent was distilled off and the condensation commenced immediately; after heating on a boiling water bath for one hour the calcium all disappeared. Two hundred cc. of petroleum ether were added and the product was extracted as usual. From the "acidification product" 10 grams of camphoroxalic acid were obtained.

Experiment 2.—The same as Exp. 1, except that 50 cc. xylene were used as the solvent.

No action resulted from heating for three hours. The solvent was distilled off and the residue again heated for two hours at 200° without result. Upon adding 50 cc. absolute alcohol and

heating at 100° for two hours the calcium was entirely dissolved. The product was extracted as in Exp. 1 and 10 grams of camphoroxalic acid were obtained.

Experiment 3.—The same as Exp. 1, except that 200 cc. of ether were used as the solvent.

No action took place during three hours at 36°. The addition of 75 cc. of pyridine produced no result.

Experiment 4.—22.8 grams camphor (1.5 mols.); 16.5 grams ethyl cinnamate (1 mol.); 4.0 grams calcium (1 mol.).

Boiling for two hours in 200 cc. hexane (b. p. 90°) produced no result. Fifty cc. of xylene were substituted for the hexane and the solution boiled for 4 hours without effect. When boiled for 4 hours at 160° without a solvent a reaction took place and part of the calcium was acted upon. The "acidification product" was a brown, semisolid mass. It was dissolved in ether and the solution extracted successively with aqueous solutions of sodium bicarbonate and sodium carbonate, cinnamic acid being thus removed. From the ethereal solution 5 cc. of a reddish brown oil were obtained which did not change after long standing. This gave a decided test with ferric chloride.

The "solvent products" obtained in the above experiment gave no tests with ferric chloride.

B. Experiments with Sodamide.

Experiment 5.—15.2 grams camphor (1 mol.); 14.6 grams ethyl oxalate (1 mol.); 3.9 grams sodamide (1 mol.).

No reaction resulted when hexane or xylene was used as solvents even when absolute alcohol was added. Upon heating for two hours without a solvent, at 150°, a reaction took place, a reddish brown mass resulting. From the "solvent" and "acidification products" were obtained 3 grams and 1 gram, respectively, of camphoroxalic acid.

Experiment 6.—The same as Exp. 5, using 200 cc. of ether and 75 cc. of pyridine as a solvent.

Boiling for 4 hours and standing at room temperature for some weeks produced no effect.

Experiment 7.—22.8 grams camphor (1.5 mols.); 15.0 grams ethyl benzoate (1 mol.); 3.9 grams sodamide (1 mol.); no solvent.

No reaction took place until the temperature was raised to 200°. The sodamide then disappeared within 5 minutes, and 5 cc. of a reddish brown oil giving a color test with ferric chloride were obtained. This gradually deposited benzoic acid. The residue consisted chiefly of ethyl benzoate. A small amount distilled at 230° to 245°. Very little condensation took place.

These experiments show that sodamide and calcium are far inferior to sodium unless the condensation takes place at a high temperature, at which the products must also be stable in order to obtain good yields.

Experiments Showing the Effect of Various Solvents and Temperatures.

A large number of condensations were carried out using as solvents varying quantities of ether, petroleum ether (b. p. 36°), ligroin (b. p. 50° to 55°), ligroin (b. p. 70° to 75°), hexane (b. p. 90°), benzene, toluene, and xylene. The esters used were ethyl formate, acetate, oxalate, benzoate, cinnamate, and phthalate. The products seemed equally soluble in all of the solvents and the solvent employed did not affect the yield of diketone obtained to any marked degree. The speed of the reaction seemed to increase with the temperature, except when ether was used as a solvent. In this case the reaction was accelerated to a marked degree, independently of the temperature.

Experiments Showing the Effect of the Esters of Various Acids upon the Condensation.

A. Aliphatic.

1. Esters of Monobasic Acids.

Experiment 9.—22.8 grams camphor (1.5 mols.); 7.4 grams ethyl formate (1.0 mol.); 2.3 grams sodium wire (1.0 atom); 300 cc. toluene.

After standing for a week at the room temperature, some of the metal remained unattacked. Consequently, the liquid was boiled for several hours. The yield of hydroxymethylenecamphor was fair.

Claisen's experiments on the preparation of hydroxymethylenecamphor were made with ether as a solvent.

Experiment 10.—22.8 grams camphor (1.5 mols.); 8.8 grams

ethyl acetate (1.0 mol.); 2.3 grams sodium wire (1.0 atom); 200 cc. ether.

The reaction commenced at room temperature, and at the end of twenty-four hours the liquid was dark brown, with a brown precipitate at the bottom. There was also a dark brown solid having the general form of the wire, but examination showed that it contained very little sodium. The flask, with its contents, was allowed to remain eight days longer at the ordinary temperature, but no further change could be detected at the end of that time. The "solvent product" consisted of a yellow liquid which gave no coloration with ferric chloride. From this some camphor crystallized. The "acidification product" was a reddish brown oil, which did not solidify when placed in a freezing mixture, nor by long standing. It gave a deep color with ferric chloride. Treatment of its ethereal solution with aqueous solutions of sodium bicarbonate, sodium carbonate, and potassium hydroxide, in the order named, failed to remove any compounds. The exact details of this attempted method of separation are described under Experiment 14.

Experiment 11.—22.8 grams camphor (1.5 mols.); 11.6 grams ethyl butyrate (1.0 mol.); 2.3 grams sodium wire (1.0 atom); 200 cc. ether.

The action commenced at once at room temperature, and appeared to be complete at the end of about twelve hours. The solution was reddish brown in color, with a dark brown precipitate, partly in the form of pieces of the wire. The "solvent product," which gave no coloration with ferric chloride, deposited unchanged camphor. The "acidification product" consisted of a reddish brown oil, which gave a deep color with ferric chloride and did not solidify. Treatment with alkali and alkaline carbonates, in the manner described under Exp. 14, failed to yield any tangible products.

2. *Esters of Dibasic Acids.*

Work with the ethyl oxalate compound is described under Experiments 1 to 6. In addition, an exhaustive study of its action on camphor has been made by J. Bishop Tingle,[1] who has also in-

[1] This Journal, **19**, 373 (1897); **20**, 318 (1898).

vestigated the behavior of the methyl, propyl, and isoamyl esters of the same acid.

Experiment 12.—22.8 grams camphor (1.5 mols.); 16.0 grams ethyl malonate (1.0 mol.); 4.6 grams sodium wire (1.0 atom); 300 cc. hexane (b. p. 90°).

A brisk evolution of hydrogen accompanied the action of the sodium upon the ester in the hexane. It commenced immediately after the introduction of the wire into the solution. A white, flocculent material soon covered the metal, and the liquid became distinctly pink. The evolution of gas ceased after twenty minutes. The product was boiled for fifteen minutes longer, which caused the disintegration of the wire and its ultimate solution. The camphor, dissolved in a small quantity of hexane, was now added, whereupon the liquid began to turn brown. After two hours' boiling the precipitate had completely disappeared and the liquid was of a deep reddish brown color. It was allowed to remain overnight at the ordinary temperature.

The "solvent product" consisted of a black liquid, containing camphor; it gave no coloration with ferric chloride. The "acidification product," which was a heavy, reddish brown oil, gave a deep coloration with ferric chloride. The yield of oil was about 2 cc.

Experiment 13.—22.8 grams camphor (1.5 mols.); 17.4 grams ethyl succinate (1.0 mol.); 2.3 grams sodium wire (1.0 atom); 250 cc. ether.

After an hour at the room temperature, the substances showed no signs of reacting; but, on boiling, the liquid became yellow and a yellow incrustation formed over the wire. At the end of eight hours' boiling the metal began to disintegrate. Heating was now stopped and the material allowed to remain at the room temperature for forty-eight hours. The "solvent product" was a red liquid, which gave a coloration with ferric chloride and deposited camphor. The "acidification product" consisted of a reddish brown oil, which formed a deep colored solution with ferric chloride.

B. Aromatic.

1. Esters of Monobasic Acids.

Experiment 14.—22.8 grams camphor (1.5 mols.); 15.0 grams

ethyl benzoate (1.0 mol.); 2.0 grams sodium wire (1.0 atom); 100 cc. hexane (b. p. 90°).

After two hours' heating on the water bath, the contents of the flask gradually became reddish brown. The material was allowed to remain overnight at the ordinary temperature. The "solvent product" consisted of a yellow oil, which did not solidify and gave no test with ferric chloride. The "acidification product" was a reddish brown oil, which formed a deep color with ferric chloride. After some days most of the compound had solidified. It was dissolved in ether and the solution well shaken with aqueous solutions of sodium bicarbonate, sodium carbonate, and potassium hydroxide, successively. The residue from the ethereal solution was dried, the ether distilled off, and the resulting reddish brown oil, which gave no signs of solidification when kept in a freezing mixture for several days, was treated in the manner described below.

The three alkaline solutions were acidified and extracted separately with ether, which was then dried and distilled. In this manner there was obtained from the sodium bicarbonate solution a relatively large quantity of benzoic acid. The sodium carbonate solution was found to have extracted benzoic acid, together with a little yellow oil. A mere trace of yellow solid was extracted from the potassium hydroxide solution. None of these substances gave any red coloration with ferric chloride.

Returning now to the purified reaction product, which gave a deep coloration with ferric chloride and weighed 3.5 grams; it was mixed with water (50 cc.), and 10 cc. aqueous sodium hydroxide solution (sp. gr. 1.15) was added. After remaining at the room temperature for forty-eight hours, the solution was red, and a reddish brown, sticky substance had deposited. The liquid was poured off, acidified with dilute sulphuric acid, and allowed to stand overnight. In this manner a small quantity of crystals was obtained; extraction of the acid liquor did not materially increase the yield of these. A small additional quantity of the compound was obtained by a second treatment of the yellow, resinous material with aqueous alkali hydroxide. The solubility of the compound did not lend itself to its ready purification. After many trials it was found that the best results

were obtained by the use of a mixture of acetone and water. In this manner, yellow, needle-shaped crystals melting at 91.5° were obtained. It gives a deep red color with ferric chloride. Analysis showed that the compound was not quite pure.

	Calculated for $C_8H_{14}<\begin{matrix}C:C(OH)C_6H_5\\ \vert\\ CO\end{matrix}$	Found.
C	79.69	81.04
H	7.81	8.14

The investigation of this substance will be continued.

A number of attempts were made to obtain compounds of camphor with the ethyl nitrobenzoates. Sodium wire, alcoholic sodium ethylate, and sodium ethylate free from alcohol were employed as the condensing agents, and the temperature conditions were varied. It was found, in each case, that the last two condensing agents attacked the nitro group more or less vigorously, depending on the temperature. With sodium wire black compounds were formed. Apparently the hydrogen eliminated by the camphor reduced the nitro group to some extent, and the resulting products oxidized more or less on exposure to air.

Experiment 15.—22.8 grams camphor (1.5 mols.); 16.5 grams ethyl cinnamate (1.0 mol.); 2.3 grams sodium wire (1.0 atom); 500 cc. ether.

After the mixture had remained during ten minutes at the ordinary temperature the reaction had become very vigorous, and in the course of five minutes more, the sodium had dissolved completely. The liquid was a deep brown and a yellow, solid precipitate had formed; it was allowed to remain during twelve hours at the ordinary temperature.

The "solvent product" consisted of a reddish brown oil, which gave a decided coloration with ferric chloride. Before acidifying, the aqueous solution was again extracted with ether, to free it from traces of borneol and camphor, and the ether remaining in the aqueous solution was removed by a current of air. Acidification with acetic acid produced a milky precipitate, which, after twenty-four hours, had gathered on the dish in the form of a yellow, sticky mass that could not be filtered. The

mother liquor was decanted and the material dried. It gave a deep coloration with ferric chloride.

2. Esters of Dibasic Acids.

Experiment 16.—22.8 grams camphor (1.5 mols.); 22.2 grams ethyl phthalate (1.0 mol.); 2.3 grams sodium wire (1.0 atom); 300 cc. ether.

Immediately after mixing the materials the wire turned dark, and in the course of a few minutes the reaction was so violent that it was necessary to moderate it by immersing the flask in ice water. The wire had completely dissolved at the end of fifteen minutes, the solution assuming a golden brown color. It was allowed to stand overnight at the room temperature.

The liquid was poured into ice water, the mixture well shaken, and the ether removed. After evaporation it left a red liquid which gave a slight coloration with ferric chloride. The aqueous solution was extracted twice with fresh portions of ether and it was then treated with a current of air, until it no longer gave an odor of ether. Dilute acetic acid (1:1) was now added in excess. A yellow, sticky substance separated immediately; it was allowed to remain in contact with the mother liquor for twenty-four hours and was then filtered. After being dried it formed a yellow resin, was readily soluble in alcohol, and gave a deep coloration with ferric chloride. The acid mother liquor was extracted with ether. This extract left a quantity of reddish brown oil which gave an intense coloration with ferric chloride. This oil, in the course of a week, changed almost completely into a white solid which gave no coloration with ferric chloride. The resinous material spoken of above also changes slowly into a white solid giving no reaction with ferric chloride. It appears as if there were here an unstable enolic and a stable ketonic form of the diketone, which produce an equilibrium mixture after the liberation of the former. The supposed ketonic form is insoluble in alcohol, ether, and benzene. The supposed enolic form is soluble in all of these. If the enolic form is dissolved away from an equilibrium mixture of the two forms, it will slowly commence to deposit more of the supposed ketonic form.

This substance is now under investigation.

INFLUENCE OF CATALYTIC AGENTS ON THE CLAISEN CONDENSATION.

Experiment 17.—22.8 grams camphor (1.5 mols.); 15.0 grams ethyl benzoate (1.0 mol.); 2.3 grams sodium wire (1.0 atom); 400 cc. petroleum ether (b. p. 36°).

An action commenced slowly at the room temperature. The wire continued bright or white for two hours, during which time a yellow precipitate deposited in the flask. The liquid now became yellow and gradually darkened, finally becoming deep red. The wire also darkened and acquired a reddish brown coating, but five days were required before it disappeared. The solution and precipitate were treated separately with water, acid, etc. About equal amounts of the "acidification products" of the solution and the precipitate were obtained. They consisted chiefly of benzoic acid, together with a reddish brown oil which gave a coloration with ferric chloride. The "solvent product" was a yellow oil which gave a coloration with ferric chloride. The yield of diketone was poor, about 4.0 grams of the crude diketone and 2.3 grams of benzoic acid being formed.

Experiment 18.—Same as Exp. 17. Added as a catalytic agent 100 cc. ether.

A reaction commenced at once, and after about an hour the solution had about the same color as described in Exp. 25, but the precipitate was not quite as heavy and the coating on the wire was much thicker. At the end of two hours all but a slender thread of sodium had disappeared; the liquid was deep red and the precipitate a very deep brown. It was allowed to remain overnight. The yield of diketone was about the same as that obtained in Exp. 17.

Experiment 19.—Same as Exp. 17. Added as a catalytic agent 75 cc. pyridine.

The liquid quickly assumed a bluish tinge, the wire acquired a dark coating, and there was a small quantity of a white, flocculent precipitate. At the end of two hours this precipitate had disappeared, but another one, almost black, had collected at the bottom of the flask. The liquid was reddish brown, and the metal had almost all reacted. The mixture was allowed to remain overnight. The yield was practically the same as in the

preceding experiments and the velocity of the reaction essentially equal to that produced by ether.

Experiment 20.—Same as Exp. 17. Added as a catalytic agent 10 cc. quinoline.

The reaction commenced at once. The liquid and wire both darkened and the metal became covered with a rough coating, a brown precipitate being also deposited on the bottom of the flask. The liquid was boiled during two hours, at the end of which time most of the metal had reacted. The product was allowed to remain overnight. The yield was practically identical with that obtained in the previous experiments.

Experiment 21.—22.8 grams camphor (1.5 mols.); 16.5 grams ethyl cinnamate (1.0 mol.); 2.3 grams sodium wire (1.0 atom); 500 cc. ether.

After remaining for ten minutes at the ordinary temperature the reaction had become quite brisk, and at the end of five minutes more the sodium had disappeared. The liquid was deep brown with a yellow solid which did not adhere to the metal. The "solvent product" consisted of a yellow oil. The "acidification product" was, at first, entirely liquid, but gradually deposited a red, sticky solid which was removed. All three products gave deep colors with ferric chloride.

Experiment 22.—The same quantities of camphor, ester, and sodium as in Exp. 29; 300 cc. petroleum ether (b. p. 36°).

Hardly any action had taken place at the end of two hours, consequently, 25 cc. of ether were added. This caused the rapid production of a red solid, the wire remaining bright throughout the experiment. At the end of two hours most of the metal had dissolved and the remainder disappeared after the mixture had been allowed to stand overnight. The yield was practically the same as in the preceding experiment.

Experiment 23.—22.8 grams camphor (1.5 mols.); 22.2 grams ethyl phthalate (1.0 mol.); 2.3 grams sodium wire (1.0 atom); 400 cc. petroleum ether (b. p. 36°).

During six hours at room temperature, the wire gradually darkened and assumed a brown coating, which then slowly deposited at the bottom of the flask. The liquid became yellow. After remaining overnight practically all the sodium had re-

acted, but much of the solid product retained the original form of the wire coils. The yield was as good as any which has been obtained.

Experiment 24.—Same as Exp. 23. Added as a catalytic agent 50 cc. ether.

The mixture without the ether was allowed to remain for an hour at room temperature. The ether was then added. The action immediately became more rapid, and at the end of three hours the metal had completely disappeared and a finely divided, dark brown precipitate had formed. This was allowed to remain during twenty-four hours at the room temperature. The yield of diketone was about equal to that previously obtained.

Experiment 25.—Same as Exp. 23. Added as a catalytic agent 10 cc. of quinoline.

In five minutes the wire became red, and at the end of three hours all of it except a thin thread had reacted. The liquid was reddish brown, and a black precipitate had formed. A good yield of the product was obtained, but it appeared to consist entirely of what is believed to be the ketonic form of the diketone. Although the reaction did not take place as rapidly as when ether was employed as the catalyst, there is no doubt as to the large accelerating influence of quinoline.

Experiment 26.—Same as Exp. 25, except that ethyl oxalate was used instead of ethyl phthalate.

The object of this experiment was to see if quinoline had any influence on the production of (enolic) camphoroxalic acid. The product, however, appeared to be identical with the ordinary form of the acid. In view of Michael's investigation of the action of tertiary bases and desmotropic compounds,[1] this result is what might be expected.

Experiment 27.—Same as Exp. 23. Added as a catalytic agent 100 cc. pyridine.

This experiment was performed to see if pyridine, as well as quinoline, tended to promote the formation of the supposed ketonic form.

At the ordinary temperature the wire and liquid immediately darkened, and a black precipitate formed. After an hour al-

[1] Ber. d. chem. Ges., **39**, 209 (1906).

most all the sodium had dissolved, and the following morning it had completely disappeared. Neither of the products of this reaction gave any coloration with ferric chloride. The catalytic influence of pyridine was plainly evident.

Investigation of Conditions Affecting the Formation of the Grignard Reagent.

The object of these experiments was to discover whether the Grignard reagent can be formed under certain conditions, at a relatively low temperature, in the absence of ether or a tertiary base. For this purpose it was, obviously, desirable to use a halogen derivative which possessed the maximum activity toward magnesium. Some of our experiments were made with ethyl chloracetate, which was found to be well adapted to our purpose.

Experiment 28.—12.0 grams ethyl chloracetate (2 mols.); 1.22 grams magnesium ribbon (1 atom); 50 cc. ether.

The reaction took place so rapidly that it was necessary to cool the materials in a freezing mixture.

Experiment 29.—This was the same as Exp. 28, except that 200 cc. petroleum ether (b. p. 36°), were used in place of the ether. No apparent action was observed after several hours' boiling, consequently a little iodine was added and the heating continued for ten hours longer. The liquid had turned yellow at the end of this time, and a yellow, crystalline precipitate coated the metal and settled to the bottom of the flask.

Experiment 30.—The conditions were the same as in Exp. 29, except that the solvent consisted of 35 cc. of ether in addition to the petroleum ether. After three hours' boiling a heavy precipitate had formed and at the end of ten hours this was largely augmented. Action was much more rapid than in the preceding experiment.

Experiment 31.—This was carried out exactly as in the case of Exp. 29, except that the solvent petroleum ether was reduced to 50 cc. Most of the magnesium had dissolved after boiling for sixteen hours. Evidently a greater concentration of the ester favors its attack on the metal.

Experiment 32.—7.80 grams ethyl iodide (1 mol.); 1.22 grams

magnesium ribbon (1 atom); 50 cc. petroleum ether (b. p. 36°); 30 cc. quinoline.

No reaction took place at the ordinary temperature, but after boiling for twenty minutes most of the metal had dissolved and a red mass formed. With benzoic aldehyde this substance gave a rather poor yield of the secondary alcohol.

Experiment 33.—This was similar to the preceding experiment, except that 25 cc. of ether were used instead of the quinoline, and the quantity of petroleum ether was reduced one half. The action commenced at the ordinary temperature, the liquid soon began to boil, and after half an hour most of the metal had dissolved. Treatment of the product with benzoic aldehyde gave an excellent yield of the secondary alcohol.

Experiment 34.—7.80 grams brombenzene (1 mol.); 1.22 grams magnesium ribbon (1 atom); 200 cc. petroleum ether (b. p. 36°); 5 cc. quinoline.

No apparent change took place after two hours boiling; consequently, a little iodine was added and the heating was continued during ten hours. A red compound was formed, which reacted only slowly with benzoic aldehyde, and the yield of secondary alcohol was poor.

Experiment 35.—This was a repetition of the preceding experiment, but 50 cc. of pyridine were used instead of the petroleum ether and quinoline. The results were similar to those recorded above, except that the metal had almost all disappeared after four hours' boiling.

Experiment 36.—A similar experiment to Exp. 34, except that the quantity of petroleum ether was reduced to 50 cc. and 15 cc. of pyridine were added as the catalytic agent. Most of the metal had dissolved after six hours' boiling. The product of the reaction was similar to those described above.

Effect of Solvents and Catalytic Agents on the Synthesis of Ethyl Acetoacetate.

Under ordinary conditions the synthesis of ethyl acetoacetate, as is well known, is carried out by the use of ethyl acetate in excess, the excess acting as the solvent. It was desired to ascertain the effect upon the reaction of the use of petroleum ether

as a solvent, and also to determine the action of catalytic agents such as ether and pyridine.

Experiment 37.—17.6 grams ethyl acetate (2 mol.); 2.3 grams sodium wire (1 atom); 50 cc. petroleum ether (b. p. 36°).

During the first half hour a slight reaction took place, some white, flocculent matter was formed and then disappeared, and there was a slight evolution of hydrogen. The liquid turned yellow gradually, but there was no further change during fourteen hours at the room temperature. After four days under the same conditions the liquid was darker. The wire retained its form, although most of the metal had reacted. The product of the reaction was treated in the manner described by Gattermann.[1] After purification a portion boiled at 175° to 177° and this gave an intense color with ferric chloride.

Experiment 38.—This was the same as the preceding experiment except that 75 cc. of ether were added. The reaction was much more rapid than before. The mixture was allowed to remain during twelve hours at the ordinary temperature, then boiled for four hours, at the end of which time all the sodium had reacted. After remaining overnight the ethyl acetoacetate was separated and identified as described above.

Experiment 39.—In this case 35 cc. of ether were employed; otherwise the conditions were the same as in Exp. 37. The reaction was more rapid and a considerable quantity of the metal was dissolved during the first hour. It was allowed to remain overnight and then boiled for four hours. The product gave the same tests as in the preceding cases.

Experiment 40.—This was also the same as Exp. 37, except that 35 cc. of pyridine were added. At the end of an hour, at the ordinary temperature, the liquid was red, with some dark colored material at the bottom. After remaining overnight it was heated for two hours, when the sodium had, apparently, all reacted. The product gave the tests previously noted.

Experiment 41.—17.6 grams ethyl acetate (2 mol.); 2.3 grams sodium wire (1 atom); 35 cc. pyridine.

A reaction commenced immediately, the wire gradually becoming red, then black and, after heating during two hours, the

[1] Organ. Prep., 2nd Am. Ed., p. 155.

sodium was completely changed. The product was freed from pyridine by washing with dilute (1:3) hydrochloric acid and subsequently distilled under reduced pressure. The purified material gave the tests for ethyl acetoacetate.

EFFECT ON THE CLAISEN CONDENSATION OF THE PRESENCE OF ALCOHOL OR OF SODIUM ALCOHOLATE.

A. Solubility of Alcoholic Sodium Ethylate and of Sodium Ethylate Free from Alcohol.

No statement has been found regarding the solubility of these substances and, consequently, some qualitative determinations have been made in order to be in a position to judge as to whether its behavior was due primarily to changes of solubility in the varying solvents employed.

The alcoholic sodium ethylate was mixed with an equal volume of each of the following substances: Dry ether free from alcohol, petroleum ether (b. p. 36°), ligroin (b. p. 80°), hexane (b. p. 90°), toluene. No precipitate formed after remaining for an hour nor on heating the liquids. In all cases the solutions remained homogeneous.

Sodium ethylate free from alcohol, in a finely powdered condition, was added, in small quantity, to separate portions of each of the following liquids: Dry ether free from alcohol, petroleum ether (b. p. 36°), ligroin (b. p. 80°), hexane (b. p. 90°), benzene, pyridine, quinoline. In no case did any appreciable quantity dissolve.

B. Experiments on the Synthesis of Ethyl Acetoacetate.

Experiment 42.—17.6 grams ethyl acetate (2 mol.); 2.0 grams sodium wire (1 atom); 50 cc. petroleum ether (b. p. 36°); 10 drops of alcoholic sodium ethylate.

An action commenced at once, the sodium turning white and the liquid darkening rapidly. After remaining for an hour at the ordinary temperature, the liquid was boiled for two hours, at the end of which time the sodium had disappeared. The product gave traces of ethyl acetoacetate, as shown by the boiling point test and the coloration with ferric chloride.

Experiment 43.—17.6 grams ethyl acetate (2 mol.); 6.8 grams sodium ethylate free from alcohol (1 mol.).

The ester was added to the sodium ethylate without removing the latter from the flask in which it had been prepared. When heated on a water bath the solid turned brown and dissolved gradually. After ten hours one half of the product was removed and tested for ethyl acetoacetate, which was found to be present only in traces. To the remaining portion of the product 50 cc. of ether were added and the heating continued for ten hours longer. There was no change in the appearance of the material, but it yielded 2.5 grams of a liquid which boiled at 175° to 177° and gave a deep coloration with ferric chloride. This yield is 27 per cent of the theoretical, whereas, by the ordinary method the yield is about 30 per cent. The increased yield in the second part of the experiment is attributed to the catalytic action of the ether and not to the extra heating.

C. Experiments with Ethyl Benzoate.

Experiment 44.—22.8 grams camphor (1.5 mols.); 15.0 grams ethyl benzoate (1.0 mol.); 2.3 grams sodium (1.0 atom); 200 cc. petroleum ether (b. p. 36°); 25 cc. alcoholic sodium ethylate.

The liquid darkened immediately, and after ten minutes began to boil. The action was complete after thirty minutes, the liquid being dark, with a reddish brown solid at the bottom of the flask. It was allowed to remain overnight. The "solvent product" was a yellow oil which gave no coloration with ferric chloride. The "acidification product" consisted chiefly of benzoic acid, together with a very little diketone. The acid was extracted by means of an aqueous solution of sodium bicarbonate.

Experiment 45.—15.0 grams camphor (1 mol.); 15.0 grams ethyl benzoate (1.0 mol.); 2.3 grams sodium wire (1.0 atom); absolute alcohol.

The metal was dissolved in four times the theoretical quantity of absolute alcohol. The camphor was dissolved in the ethyl benzoate. The solutions were mixed, but no visible reaction took place. Heating on a water bath caused the deposition of a white, solid cake, which was completely dissolved at the end of two hours, the solution becoming gradually dark. The "solvent product" was similar to that obtained in the pre-

ceding experiment. The "acidification product" consisted of a red oil which gave no characteristic coloration with ferric chloride. It proved to consist almost entirely of ethyl benzoate, together with traces of benzoic acid.

Experiment 46.—22.8 grams camphor (1 mol.); 15.0 grams ethyl benzoate (1 mol.); 2.3 grams sodium wire (1 atom); 6.9 grams dry sodium ethylate; 200 cc. petroleum ether (b. p. 36°).

After mixing the materials the liquid became slightly dark at the ordinary temperature, during the course of an hour. It was allowed to remain overnight without heating, and was then dark brown, with a heavy, yellow precipitate. Most of the sodium had disappeared. The contents of the flask were treated in the usual manner. The "solvent product" resembled that in the two preceding experiments. From the "acidification product" some benzoic acid separated, together with 1.2 grams of diketone.

Experiment 47.—This was the same as Exp. 44, except that 25 cc. of absolute alcohol were used in the place of the same volume of alcoholic sodium ethylate. The reaction commenced at once and the liquid began to boil violently at the end of three minutes, so that it was necessary to immerse the flask in ice water. The action appeared to be complete after fifteen minutes. The "solvent product" resembled that obtained in Exp. 44. The "acidification product" consisted chiefly of ethyl benzoate, together with a relatively large quantity of benzoic acid. The quantity of diketone formed was very small.

D. Experiments with Ethyl Phthalate.

Experiment 48.—22.8 grams camphor (1.5 mols.); 22.2 grams ethyl phthalate (1 mol.); 2.3 grams sodium wire (1 atom); 400 cc. petroleum ether (b. p. 36°); 25 cc. alcoholic sodium ethylate.

A reaction commenced immediately, the wire and the liquid both turning dark. After fifteen minutes at the room temperature about half of the wire had dissolved. Action appeared to be practically complete at the end of two hours. The liquid was dark red, most of the wire had disappeared, and the remainder had entirely disintegrated. The "solvent product" was a yellow oil. Both it and the "acidification product" gave

a red color with ferric chloride, but the yield of the "acidification product" was only about one half of that obtained, under similar conditions, by the use of ether or a tertiary base as a catalytic agent.

Experiment 49.—This was the same as Exp. 48, except that only two drops of alcoholic sodium ethylate were employed. About four hours were required to complete the reaction. The product and the yield were practically the same as in the preceding experiment.

Experiment 50.—This was the same as Exp. 48, except that the alcoholic sodium ethylate was replaced by an equal volume of absolute alcohol. The sodium wire remained light colored for two minutes and then commenced to darken rapidly; two minutes later it was brown and the liquid reddish in color, and there was a considerable evolution of gas or vapor from the neighborhood of the wire. Fifteen minutes after the experiment was commenced the metal had disappeared and the liquid had assumed a deep reddish tint. It was allowed to remain overnight at the ordinary temperature. The "solvent product" was a yellow oil, which gave no coloration with ferric chloride. The "acidification product" consisted of about 3 cc. of a reddish brown oil, giving a deep color with ferric chloride. The oil rapidly changed to a white solid. The yield of condensation product was much smaller than that obtained in Exp. 48, where alcoholic sodium ethylate was used.

These results show that although a reaction is rapidly brought about by the use of alcoholic sodium ethylate, and even more rapidly by the use of absolute alcohol, yet the yield of diketone is diminished in every case and relatively large quantities of benzoic acid are obtained. Apparently no phthalic acid is formed under similar conditions. It is hoped that more light on this interesting point will be gained in a subsequent investigation.

The Effect of Varying Quantities of Sodium on the Yield of Diketone.

These experiments were carried out in connection with the ones described in the following section. Those esters were se-

lected which had been found to react the most readily with sodium. Bishop Tingle has described some work regarding the effect produced on the yield of camphoroxalic acid by varying proportions of sodium, and J. Wislicenus[1] studied the action of sodium, in excess, on ethyl acetate.

Experiment 51.—7.9 grams camphor (1 mol.); 7.3 grams ethyl oxalate (1 mol.); 4.6 grams sodium wire (4 atoms); 250 cc. hexane (b. p. 90°).

The wire was added to the ester and the solvent, and the mixture heated for about fifteen hours. At the end of this time the metal had reacted. The liquid was reddish brown and a red precipitate had formed. The camphor, dissolved in the remaining hexane, was now poured in and the heating continued for four hours. Most of the solid dissolved. The "acidification product" gave 5.3 grams of camphoroxalic acid, or 43 per cent of the theoretical yield. This is only about half the average yield obtained when one atomic proportion of sodium is added.

Experiment 52.—7.6 grams camphor (1 mol.); 7.3 grams ethyl oxalate (1 mol.); 2.3 grams sodium wire (2 atoms); 250 cc. ether.

Only one half the above quantity of sodium was added at first to the ester and the solvent. The reaction proceeded as in Exp. 51. The ether did not appear to affect the speed of the reaction between sodium and the ester. After heating during two hours on a water bath the wire retained its shape; the liquid was yellow, and a precipitate of the same color had formed. The remaining sodium was now added together with the camphor, the solution having been cooled to the room temperature. At the end of three minutes the liquid boiled and in twenty minutes the action ceased, although much of the wire still held its shape. The product was boiled for twenty minutes more and allowed to remain at room temperature for twelve hours. This treatment produced no visible change. Before the addition of the product to water and acid, about a gram of unchanged sodium was removed. The yield of crude camphoroxalic acid was 5.5 grams, which is 58 per cent of the theoretical.

[1] Ann. Chem. (Liebig), **186**, 193 (1877).

Experiment 53.—7.6 grams camphor (1 mol.); 8.0 grams ethyl malonate (1 mol.); 2.3 grams sodium wire (2 atoms); 250 cc. hexane (b. p. 90°).

As soon as the evolution of hydrogen, caused by adding the sodium to the ester and solvent, had ceased, the mixture was heated on a water bath during four hours, and then allowed to remain overnight at the ordinary temperature. A white, flocculent compound was present in the liquid, but much of the wire was unchanged. The mixture was boiled on a sand bath during twenty hours, at the end of which time about one half of the wire was unchanged. The liquid was yellow and the precipitate brown. The camphor, dissolved in hexane, was now added and the heating continued for four hours. The product was allowed to stand overnight. Some of the sodium was still unchanged; the liquid was a deep reddish brown, with a dark precipitate present. The "acidification product" consisted of 3.8 grams of a reddish brown oil which gave an intense color with ferric chloride.

Experiment 54.—8.75 grams sodium camphor (1 mol.); 8.00 grams ethyl malonate (1 mol.); 2.30 grams sodium wire (2 atoms); 300 cc. petroleum ether (b. p. 36°); 50 cc. ether.

The ester, one half the sodium, and the petroleum ether were mixed and allowed to remain at the room temperature during twelve hours. The mixture was then boiled for two hours, when the metal was dissolved. The remaining sodium was now added and the boiling continued. A yellow solid formed gradually. More sodium was then put in, but as it remained unchanged it was removed later. The sodium camphor and ether were now added. After boiling for six hours the solid was a deep brown. It was allowed to remain overnight. The "acidification product" consisted of 2.4 grams of oil, which gave an intense coloration with ferric chloride.

Experiment 55.—22.8 grams camphor (1.5 mols.); 15.0 grams ethyl benzoate (1 mol.); 2.3 grams sodium wire (1 atom); 50 cc. hexane (b. p. 90°).

The camphor, sodium, and solvent were mixed and heated for an hour. The product was light yellow, but on adding the ester it rapidly became brown. It was heated for another

hour. The "acidification product" was a white solid (benzoic acid), with a little reddish brown oil. The yield of diketone was poor.

Experiment 56.—11.4 grams camphor (1.5 mols.); 7.5 grams ethyl benzoate (1 mol.); 2.3 grams sodium wire (2 atoms); 300 cc. ligroin (b. p. 70°); 50 cc. ether.

After remaining for three hours at the ordinary temperature the wire was dark brown; it was boiled during four hours and allowed to remain overnight. The liquid was yellow and a brownish yellow precipitate had formed. After being heated for two hours longer and allowed to remain at the ordinary temperature for twenty-four hours, the wire had almost completely changed and most of the product was in solution. The "acidification product" consisted of 5.3 grams of a yellow solid, from which 2 grams of benzoic acid were separated by means of an aqueous solution of sodium bicarbonate, after dissolving the product in ether. The residual diketone weighed 0.7 gram. The "solvent product" was distilled with steam. The volatile material consisted of 2.1 grams of benzyl alcohol and 6.0 grams of a mixture of camphor and borneol. The nonvolatile portion failed to react with phenylhydrazine or with *m*-nitrobenzoyl chloride and alkali.

Experiment 57.—This was a duplicate of the preceding experiment, except that twice as much sodium wire was employed. The reaction proceeded in the manner described. The "solvent product" yielded a little camphor and borneol, but only traces of benzyl alcohol. The "acidification product" consisted of 8.3 grams of solid, which gave 2.7 grams of benzoic acid and 2.2 grams of crude diketone.

Experiment 58.—The quantities of substances used were the same as in Exp. 57, but the two atomic proportions of sodium were allowed to react with the ester. After two hours' heating the liquid was yellow, with a red precipitate present; the wire was golden brown. The heating was continued for six hours longer, when the precipitate was light brown and the liquid yellow. Almost all of the sodium had reacted. The camphor was now added and the heating continued dur-

ing seven hours. The solvent was yellow and the precipitate a deep reddish brown. The "solvent product" gave 4.4 grams of camphor and borneol, and only traces of benzyl alcohol. The "acidification product" consisted of 12.8 grams of reddish brown oil, from which 3.8 grams of benzoic acid and 1.0 gram of crude diketone were separated.

Experiment 59.—7.6 grams camphor (1 mol.); 7.5 grams ethyl benzoate (1 mol.); 6.9 grams sodium wire (3 atoms); 300 cc. ligroin (b. p. 70°); 50 cc. ether.

The ester was treated with two thirds of the sodium and the camphor with the remainder. In neither case did the ether appear to exert a catalytic influence. When the products were mixed no change took place at the ordinary temperature. After heating during seven hours, the liquid was reddish brown, with a dark brown precipitate present. The "solvent product" was a yellow oil, consisting mainly of the higher-boiling solvent. Benzyl alcohol could not be detected. The "acidification product" consisted of 7.5 grams of a reddish brown oil, from which 3.0 grams of benzoic acid and 4.4 grams of the crude diketone were obtained.

ACTION OF SODIUM ON ETHYL BENZOATE.

Bouveault's interesting work on the interaction of sodium and the aliphatic esters has been referred to previously. The action of sodium on ethyl benzoate has been investigated by Claisen and others. The main object of these experiments was to try to gain additional knowledge regarding the nature and reaction of the products formed from the metal and ester.

Experiment 60.—13.7 grams ethyl benzoate (1 mol.); 2.1 grams sodium wire (1 atom); 19.85 grams absolute alcohol; 200 cc. petroleum ether (b. p. 36°).

An action commenced at once. Hydrogen was, of course, evolved and the solution darkened rapidly. At the end of an hour most of the metal had reacted; the solution was reddish brown and a light colored precipitate was present. The flask was allowed to remain at room temperature for two hours longer. The "solvent product" consisted of a yellow oil from which 9.7 grams of ethyl benzoate were obtained, but

no benzoic acid. The "acidification product" gave 2.6 grams of benzoic acid, equivalent to 2.3 grams of the ester. This leaves 0.9 gram of the ester unaccounted for.

Experiment 61.—15.0 grams ethyl benzoate (1 mol.); 4.6 grams sodium wire (2 atoms); 4.6 grams absolute alcohol (1 mol.); 2.3 grams sodium wire (1 mol.), to form sodium ethylate; 14.2 grams camphor (1 mol.); 200 cc. ligroin (b. p. 90°); 50 cc. ether.

The solvent and the alcohol were mixed and 4.6 grams of sodium wire (2.0 mols.) added. After heating for three hours reaction had ceased and a white precipitate had deposited in the bottom of the flask. The product was cooled to room temperature and the ethyl benzoate was poured in. The remaining wire gradually became yellow and then brown. At the end of an hour the solution was yellow and a heavy white precipitate was observed in the bottom of the flask. The coil of wire was brown. After boiling during two days the metal had all disappeared. A second atomic proportion of sodium was now added and the heating continued for two days longer. This caused almost all of the wire to react. A third atomic proportion of sodium was placed in the flask and the heating prolonged during several days, but no further appreciable reaction took place. The solution was now a reddish brown, with a bulky precipitate which, as seen through the solution, appeared to be yellow in color. The camphor, dissolved in some ligroin and ether, was now added to the product of the reaction and the heating continued for four hours. The "solvent product" was a yellow oil. The "acidification product" consisted of 5.6 grams of benzoic acid and 1.4 grams of crude diketone. The quantity of the acid is equal to 7.2 grams of the ester.

Experiment 62.—15.0 grams ethyl benzoate (1 mol.); 4.6 grams sodium wire (2 atoms); 200 cc. petroleum ether (b. p. 36°).

The ester, solvent, and half of the sodium were heated during eight hours, at the end of which time the metal had disappeared. The remainder of the sodium was then added, and the heating continued for ten hours longer. This portion of

the wire also dissolved, but there was no reaction when a third atomic proportion of the metal was added and the heating prolonged for another ten hours. The "solvent product" consisted of 0.7 gram of a yellow, amorphous solid. The "acidification product" contained 5.4 grams of benzoic acid, in addition to an amorphous substance from which no crystalline derivative could be obtained by the action of benzoyl chloride (cf. Exp. 66). Allowing for the unavoidable loss in the separation and purification, the above quantity of benzoic acid is equal to one-half of the ester used, the exact ratio being 6 grams of acid: 7.5 grams of ester.

Experiment 63.—7.5 grams ethyl benzoate (1 mol.); 2.3 grams sodium wire (2 atoms); 250 cc. ether.

The reaction commenced immediately and at the end of an hour a brown precipitate began to form. The heating was continued during three days, two additional atomic proportions of sodium being added, but these apparently were not attacked. The "solvent product" consisted of 0.5 gram of a yellow oil, containing some white crystals. The "acidification product" yielded 3.9 grams of benzoic acid, equivalent to 5 grams of the acid. Speaking generally, this experiment presented the same features as those in which camphor and ethyl benzoate were condensed.

Experiment 64.—7.5 grams ethyl benzoate (1 mol.); sodium hydroxide (4 mols.); 250 cc. ether.

The hydroxide was equivalent to the total quantity of sodium used in the preceding experiment. It was dissolved in ice water and shaken with the ester, dissolved in the ether. The time occupied in the manipulation and the other conditions were exactly the same as those in Exp. 63. The "solvent product" consisted of 7.1 grams of ethyl benzoate, and the "acidification product," when dissolved in ether and treated with aqueous sodium bicarbonate, yielded 0.1 gram of benzoic acid, equivalent to 0.123 gram of the ester, thus leaving only 0.277 gram of the ester unaccounted for. This result shows that practically none of the benzoic acid which separated in the experiments described above can be formed as a result of the hydrolysis of ethyl benzoate during the extraction processes.

Experiment 65.—The "solvent products" from five different experiments with ethyl benzoate and camphor, under varied conditions, which had given very poor relative yields of diketone, were combined and distilled with steam. The volatile material was separated from the water, dried, and filtered. The solid consisted of 20 grams of a mixture of camphor and borneol. The liquid portion, after being fractionated, yielded 40 grams of benzyl alcohol, which is equivalent to about half of the ethyl benzoate employed.

Experiment 66.—3.75 grams ethyl benzoate (1 mol.); 1.15 grams sodium wire (2 atoms); 200 cc. ether.

The solid product of the reaction, which was carried out in the manner described under Exp. 63, was filtered quickly, washed several times with ether, in a closed flask, and the red solid obtained suspended in ether. Excess of *m*-nitrobenzoyl chloride and aqueous alkali were now added and the mixture shaken thoroughly. A compound deposited gradually as yellow crystals, which, after purification, melted above 310°. This substance was dissolved in 50 per cent alcohol, excess of aqueous sodium hydroxide added, and the liquid allowed to remain at the room temperature during two days. When acid was added to the solution a heavy, white precipitate was formed. This melted at 141° to 142° and was, therefore, identified as being *m*-nitrobenzoic acid. No benzoin was isolated, but the yellow compound of high melting point described above was prepared synthetically from *m*-nitrobenzoyl chloride and benzoin, in the presence of an alkali.

The results described above confirm the conclusion that, in addition to sodium ethylate, sodium and benzoic ester yield the compound $\begin{matrix} C_6H_5CONa \\ \| \\ C_6H_5CONa \end{matrix}$, which, with water, gives sodium benzoate and benzyl alcohol, in equimolecular proportions. Under suitable conditions, however, the hypothetical hydrolysis product, $\begin{matrix} C_6H_5COH \\ \| \\ C_6H_5COH \end{matrix}$, changes into benzoin, $C_6H_5CH(OH)COC_6H_5$, which was isolated in the form of its *m*-nitrobenzoyl compound.

The results also demonstrate that this reaction between the metal and the ester is by far the preponderant one under all the rather varied experimental conditions which have been employed.

The work described in the preceding pages was carried out at the University of Rochester, N. Y., and at the Johns Hopkins University. It will be continued by us during the coming academical year.

McMaster University,
Toronto, Canada.
July, 1907.

[Contributions from the Chemical Laboratory of the University of Illinois.]

REACTIONS OF THE ARSINES.

By William M. Dehn.

In an earlier contribution[1] it was held that the reactions of the arsines and their derivatives can be divided into two general classes, *viz.*, those that involve

(1) Addition.

(2) Addition and subsequent dissociation; in other words, these reactions result from alternate changes of

(1) Trivalent arsenic to pentavalent arsenic, and

(2) Pentavalent arsenic to trivalent arsenic.

The oscillations of the arsenic valencies are best illustrated by the following reactions:

Halogen-Alkyl Series (*A*).

	(*a*)			(*b*)		(*c*)	
I.	AsX_3	+ RX	$\rightarrow$	$RAsX_4$[2]	$\rightarrow$	$RAsX_2$	+ X_2[3]
	AsX_3	+ RX	$\leftarrow$	$RAsX_4$[5]	$\leftarrow$	$RAsX_2$	+ X_2[4]
II.	$RAsX_2$	+ RX	$\rightarrow$	R_2AsX_3[6]	$\rightarrow$	R_2AsX	+ X_2[7]
	$RAsX_2$	+ RX	$\leftarrow$	R_2AsX_3[9]	$\leftarrow$	R_2AsX	+ X_2[8]
III.	R_2AsX	+ RX	$\rightarrow$	R_3AsX_2[10]	$\rightarrow$	R_3As	+ X_2[11]
	R_2AsX	+ RX	$\leftarrow$	R_3AsX_2[13]	$\leftarrow$	R_3As	+ X_2[12]
IV.	R_3As	+ RX	$\rightarrow$	R_4AsX[14]			
	R_3As	+ RX	$\leftarrow$	R_4AsX[15]			

[1] This Journal, **35**, 5.
[2] See page 121.
[3] Evident in the presence of sodium.
[4] Ann. Chem. (Liebig), **107**, 274.
[5] *Ibid.*, **107**, 274.
[6] See page 107.
[7] Evident in the presence of sodium.
[8] Ann. Chem. (Liebig), **107**, 266.
[9] *Ibid.*, **107**, 269.
[10] Probable.
[11] Evident in the presence of sodium.
[12] Ann. Chem. (Liebig), **89**, 330; **112**, 231.
[13] *Ibid.*, **89**, 330.
[14] *Ibid.*, **112**, 230. Compt. rend., **39**, 541; **49**, 87. This Journal, **33**, 115.
[15] Ann. Chem. (Liebig), **89**, 311.

It will be observed that columns (*a*) and (*c*) involve trivalent arsenic, and column (*b*) pentavalent arsenic. Now, since it can be demonstrated that the compounds given are really formed in the order indicated, it is concluded that continuous progress through reactions I. to IV. involves a *regular alternation of tri- and pentavalent arsenic.*

This operation of a variable valency is further illustrated by the following

Hydrogen-Halogen-Alkyl Series (B).[1]

	(*a*)			(*b*)			(*c*)	
I.	AsH_3	+ RX	$\longrightarrow$	$RAsH_3X$[2]	$\longleftarrow$	$RAsH_2$	+ HX[3]
II.	AsH_3	+ RX	$\longrightarrow$	$RAsH_3X$	$\longrightarrow$	RAsHX	+ H_2[4]
III.	$RAsH_2$	+ RX	$\longrightarrow$	R_2AsH_2X[5]	$\longleftarrow$	R_2AsH	+ HX[6]
IV.	$RAsH_2$	+ RX	$\longrightarrow$	R_2AsH_2X	$\longrightarrow$	R_2AsX	+ H_2[7]
V.	RAsHX	+ RX	$\longrightarrow$	R_2AsHX_2[8]	$\longleftarrow$	R_2AsH	+ X_2[9]
VI.	RAsHX	+ RX	$\longrightarrow$	R_2AsHX_2	$\longrightarrow$	R_2AsX	+ HX[10]
VII.	R_2AsH	+ RX	$\longrightarrow$	R_3AsHX[11]	$\longrightarrow$	R_3As	+ HX[12]
				R_3AsHX	$\longleftarrow$	R_3As	+ HX[13]
VIII.	R_2AsX	+ RX	$\longrightarrow$	R_3AsX_2[14]	$\longrightarrow$	R_3As	+ X_2[16]
	R_2AsX	+ RX	$\longleftarrow$	R_3AsX_2[15]	$\longleftarrow$	R_3As	+ X_2[17]
IX.	R_3As	+ RX	$\longrightarrow$	R_4AsX[18]			
	R_3As	+ RX	$\longleftarrow$	R_4AsX[19]			

From the fact that most of the indicated reactions have been studied, and that their courses proceed as indicated by the arrows, general reversibility of reaction is very improbable.

Reactions I(*a*) and I(*c*) both yield the same product, $RH_2As\langle^{H}_{X}$, which decomposes as indicated in II(*b*). Reactions III(*a*) and III(*c*) yield the compound $R_2HAs\langle^{H}_{X}$,

[1] It may be observed here that arsenic, unlike nitrogen, has a greater affinity for halogen than for hydrogen, and also for alkyl than for halogen or halogen acid.

[2] Not studied, but very probable, from analogy to the formation of primary arsine.

[3] *Vide* THIS JOURNAL, **33**, 126; see pages 107 and 115.

[4] *Ibid.*

[5] *Vide ibid.*, **33**, 128; see page 107.

[6] *Vide ibid.*, **35**, 22–24.

[7] *Ibid.*

[8] Not studied.

[9] THIS JOURNAL, **35**, 14–18.

[10] *Ibid.*

[11] *Ibid.*, **35**, 18–19; see pages 121, 122 and 123.

[12] *Ibid.*

[13] Not studied, but very probable.

[14] THIS JOURNAL, **35**, 1.

[15] Ann. Chem. (Liebig), **112**, 228.

[16] Evident in the presence of sodium.

[17] Ann. Chem. (Liebig), **112**, 228.

[18] *Ibid.*

[19] *Ibid.*, **89**, 321. Also cf. page 112.

and this decomposes as shown in IV(*b*). Reaction V(*c*) and probably V(*a*) yield the product $R_2HAs\langle^{X}_{X}$, which decomposes as indicated in VI(*b*). Reactions VII(*a*) and VII(*c*) yield the compound $R_2As\langle^{H}_{X}$, which decomposes as represented in VII(*b*). Reactions VIII(*a*) and VIII(*c*) yield the product $R_2As\langle^{X}_{X}$, which probably reversibly decomposes as indicated in VIII(*a*). Reaction IX(*a*) yields the compound $R_2As\langle^{R}_{X}$, which decomposes as indicated in IX(*b*).

Now, since reactions I(*a*), III(*a*), VII(*a*), and VIII(*a*), as well as IX(*a*), all yield the compound R_4AsX in the presence of an *excess* of alkyl halide, it is concluded that the arsonium compound is formed by a series of *intermediate reactions involving molecular compounds which immediately or slowly dissociate, and that the process is repeated until the stable end products are formed.*[1]

As the result of a number of years of observation and study of the reactions of arsenic, the conviction has grown that the activity of this element cannot always be explained on the basis either of ionic or of kinetic-molecular mechanics. Briefly considered, this conviction has resulted from observation of the facts (1) that *most of the arsenic reactions are nonelectrolytic* or, in other words, they take place in the absence of water and (2) that, between the starting compounds and the most easily separated end product, there are observed *other* and

[1] Analogous alternations of valency and formation of intermediate compounds are recognized in the reactions of the amine, phosphine, and stibine derivatives, as, for instance: (1) in the Hoffmann series of reactions, when alkyl iodides and ammonia are heated together and form a mixture of the four classes of amines; (2) when alkyl iodides are heated with phosphonium iodide in the presence of zinc oxide and form a mixture of primary and secondary phosphines; and (3) when alkyl iodides are treated with sodium antimonides and form tertiary and quaternary stibines. Ease of dissociation of the various molecular compounds determines the yields of the respective derivatives; in general, with the element nitrogen *primary* amines are formed in greater quantity; with phosphorus, *primary and secondary* phosphines; and with arsenic and antimony, the respective *quaternary* compounds are obtained in greater quantity.

usually *crystalline products*, which often can be separated and analyzed. Mention of these intermediate products has been made in previous contributions;[1] a systematic study is made herein to establish their frequent formation and to secure evidence leading to the general conclusion that *compounds of the element arsenic react largely by initial coalescence with the reagent.*

Whereas the nitrogen-organic and the oxygen-organic compounds yield intermediate products, their unstable properties and usually liquid condition prevent their easy and systematic study. The arsenic-organic compounds, on the other hand, containing the heavy element arsenic, usually form *crystalline* intermediate products which can often be separated and analyzed and therefore the arsenic derivatives offer a productive field for the study of chemical statics and dynamics.

Let us consider first, by way of illustration, the spontaneous oxidation of methylarsine by means of atmospheric oxygen:

$$CH_3AsH_2 + O_2 = CH_3AsO + H_2O,$$
$$2CH_3AsH_2 + 3O_2 = 2CH_3AsO(OH)_2.$$

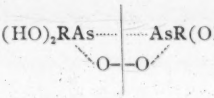
The first reaction is instantaneous, but the second is incomplete even after two weeks.

If applied here, Engler's theory of autoxidation[2] should involve *an initial addition of a molecule of oxygen*: $RH_2As\langle^{O}_{O}$. This "moloxide," by elimination of water, gives the end products, water and methylarsine oxide, RAs = O. It is not impossible, however, that the above peroxide form suffers a molecular rearrangement into the compound $RAs\langle^{OH}_{OH}$ before splitting off water; confirmation of the probable formation of an addition product of the arsine and oxygen was deduced (1) from the observed absence of condensed vapors of water, proportional to the theoretical quantity, and (2) from the *slow* formation of methylarsonic acid, which, in accord-

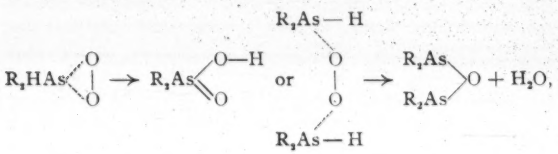
[1] See THIS JOURNAL, **33**, 101; **35**, 1. J. Am. Chem. Soc., **28**, 347.

[2] C. Engler und J. Weissberg: Kritische Studien über die Vorgänge der Autoxydation (1904), 63.

ance with Engler's theory, could be formed in the manner indicated below:

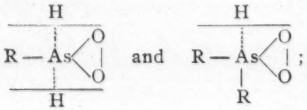


The analogous autoxidations of secondary arsines[1] are easily accounted for in the same manner:



the addition of one molecule of oxygen to one molecule or to two molecules of the arsine determining whether cacodylic acid or cacodylic oxide is formed.[2]

The molecular rearrangement of the above-mentioned compounds, RH_2AsO_2 and R_2HAsO, to form the compounds $R-As(OH)_2O$ and $R_2AsO(OH)$, necessitates a *shifting of the hydrogen atoms*[3] *and a rearrangement of the oxygen valencies*, unless it is assumed that kinetic or ionic dissociations first take place as indicated below:



and that these dissociated parts readjust themselves.

[1] This Journal, **35**, 9.

[2] Usually the two compounds are formed in nearly equal quantities. This Journal, **35**, 14.

[3] Atomic shifting, an assumption not new in chemical statics and dynamics, cannot, of course, be dispensed with as an explanation of many reactions, particularly those included under tautomeric forms.

The latter hypothesis is unnecessary and, in fact, is untenable because it *assumes an effect without providing a probable cause*. We have only to conceive that the atoms of hydrogen, by virtue of kinetic motion and while being continuously held within the spheres of attraction,[1] pass to the intersection of the spheres of oxygen and arsenic attractions (Fig. I.), and then beyond the appreciable attraction of arsenic (Fig. II.). In this manner we come to an easy understanding of atomic shifting without employing any new theories or resorting to other than the fundamental assumptions of the science.

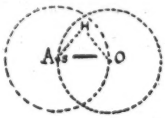


Fig. I.

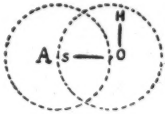
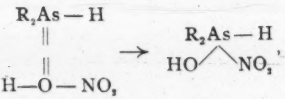


Fig. II.

That *molecular coalescence is the inevitable preliminary condition of arsine reactions* is confirmed by the behavior of dimethylarsine with nitric acid.[2] *Normal* nitric acid (1 mol.) does not react with the arsine although the mixture is heated for one hour at 125°; *concentrated* nitric acid (1 mol.) reacts with explosive violence. In the former case, the nitric acid is *ionized*; in the latter, its condition is *molecular*. In other words, the compound H—O—NO_2 has, but the group —O—NO_2 has not, the property of *adding to the arsine* and of yielding the end product, cacodylic acid. If the doubly bound oxygen atoms of the nitrate group were the active portion, then both ionic and molecular nitric acid should react; however, since only molecular nitric acid reacts, only the H—O—N part of the acid offers hope of a satisfactory explanation. If initial molecular coalescence is the indispensable criterion, then the following preliminary mechanics are conceivable:

[1] Mechanical arrangements and invariability of quantity and position are, of course, improbable conceptions of valency.

[2] This Journal, **35**, 27.



dimethylarsine nitrate[1] being first formed.

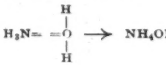
Since the formation of the analogous *arsine salt*,

$$[(CH_3)_2AsH]_2.H_2SO_4,$$

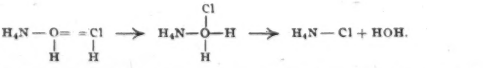
was proven in the case of sulphuric acid,[2] the probable forma-

[1] Objections may be raised as to the structure of this salt, on the grounds that it is not strictly analogous to the structure of ammonium nitrate, $H_4N—O—NO_2$; however, there is no evidence that these salts are strictly analogous. The fact that hydroxyl attached to arsenic constitutes a more stable combination than hydrogen attached to arsenic, the reverse being true in the case of nitrogen, argues a difference in these salts.

Since, in the case of ammonia and hydrochloric acid, at least a trace of water is necessary (Hughes: Phil. Mag., **35**, 53; Baker: J. Chem. Soc., **65**, 611) to form ammonium chloride, it is usually held that ionized hydrochloric acid adds to ammonia; of course, kinetic dissociation is precluded for the reason that hydrochloric acid does not begin to dissociate below 1000° (Ber. d. chem. Ges., **6**, 423). However, initial ionic or kinetic dissociations are not the only possible explanations of these phenomena; the water that is necessary may add in the following manner:

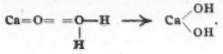


and then the acid and base may react, either through their ions, or as indicated below:



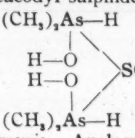
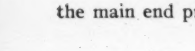
That the ions of water first add to ammonia is rendered improbable from the fact that *NH_3 itself is not an ion*.

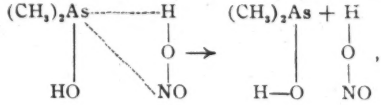
When water acts on calcium oxide and other oxides of both metals and nonmetals, it is difficult to conceive of the mechanics of the action on the basis of ionization since the oxides themselves are not ions and water is ionized to the extent of only 2 mg. of hydrogen to a ton of water. Furthermore, kinetic action is precluded because water does not decompose below 1000°. In accordance with the above principles, however, the action is readily explained as follows:



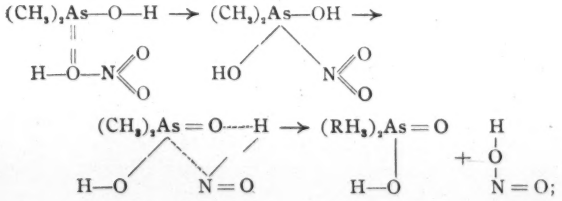
Whereas *molecular affinity* is recognized in hydrated salts and other compounds, its rational application here necessitates an assumption of the *tetravalency* of oxygen. The position of oxygen in the periodic system, the variability of valency of its closest analogue, sulphur, and the necessary postulate of a higher valency of oxygen to explain water of crystallization and the addition products of alcohols, ethers, etc., clearly entitles oxygen to an occasional higher valency than two.

[2] THIS JOURNAL, **35**, 24.

tion of the nitrate is easily deduced. The sulphate gave, as the main end products, cacodyl sulphide (and cacodylic acid), therefore, the structure  is probable, *sulphur being bound to arsenic*. Analogously, *nitrogen is probably bound directly to arsenic*, as is shown in the formula  . Under the influence of heat[1] (internal kinetic dissociation), this compound could split off nitrous acid,



forming dimethylhydroxylarsine,[2] which would react with more nitric acid, as follows:



and thus satisfactorily explain the formation of cacodylic acid, the main end product.

The above described action of nitric acid illustrates that

[1] It must be remembered that dissociations may be induced not only by heat, light, and other forces, but also by various reagents. Since the latter really involve other chemical changes the term *dissociation* is used herein to indicate decompositions induced by heat only.

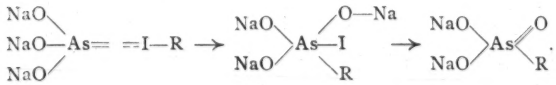
[2] This compound probably has no separate existence since, under conditions favoring its formation, its anhydrous form, cacodylic oxide, $R_2AsOAsR_2$, is always obtained (Baeyer: Ann. Chem. (Liebig), **107**, 282). However, since cacodylic oxide is proved (THIS JOURNAL, **38**, 9–14) to be an oxidation product of dimethylarsine the above conclusions are justified.

the process of oxidation is conditioned, not by the mere presence of oxygen but by a facility of coalescence of the reagent with the substance; in other words, the reducing power of the arsines and their derivatives is conditioned by a capacity for preliminary molecular linking; at any rate, most reduction processes of the arsines thus far studied[1] have yielded initial molecular aggregates, or have given evidence of their formation.

A striking example of this action of the arsenic atom is observed in the formation of arsonic acids, when sodium arsenite is treated with alkyl iodides. The reaction

$$Na_3AsO_3 + RI \longrightarrow RAsO_3Na_2 + NaI$$

was discovered by Meyer[2] and was described by him as "an anomalous reaction," because by "double decomposition" it was expected that an alkyloxy compound would be formed. However, it was found that the alkyl group combines directly with the arsenic. This is easily explained on the basis of initial molecular attraction; the arsenite and the halide uniting, rearranging, and decomposing as follows:



Thus it is seen that instead of being an "anomalous reaction" it may be considered a beautiful example of the *normal reaction*.

From the foregoing it is concluded that many reactions of the arsine compounds can best be explained by making the following assumptions:

1. Unsaturated valencies (partial or latent valencies) in both substances;
2. Molecular coalescence of the two substances;
3. A condition of instability established in the molar aggregate, owing to this distribution of the total valencies of the nuclear elements, and thus inducing either
4. A tendency toward reversible reaction or
5. A tendency toward rearrangement; and finally,

[1] See page 97.

[2] Ber. d. chem. Ges., **16**, 1441.

6. A dissociation of the molar aggregate into its more stable components.

EXPERIMENTAL.

1. Electrolytic Reduction of Arsine Derivatives.

These experiments were undertaken for the purpose of demonstrating the formation of intermediate products when alkyl arsenic derivatives are reduced to free arsines. It was found hitherto that the final reduction product of both cacodyl chloride[1] and cacodyl[2] is dimethylarsine; it is now proposed to show that cacodyl is an intermediate product of the reduction of cacodyl chloride, and that the successive reactions are as follows:

$$2(CH_3)_2AsCl + 2H = (CH_3)_2As—As(CH_3)_2 + 2HCl,$$
$$(CH_3)_2As—As(CH_3)_2 + 2H = 2(CH_3)_2AsH.$$

After a number of unsuccessful experiments with porous cells used to keep the anode and cathode solutions separate, a cell was devised which was found most convenient, not only for observing the progress of the reductions but also for experimenting with small quantities of material. The apparatus used is shown in Fig. III.

The other details are as follows: (*a*) platinum cathode spiral, (*b*) porous clay partition, (*c*) a packed asbestos ring, (*d*) platinum anode plate, (*e*) glass support for the anode plate, (*f*) exit for anode gas and intake for anode solution, (*g*) drain for anode solution, (*h*) exit for cathode gas, (*i*) intake for cathode solution.

Method of Using.—The cathode solution first used was prepared by mixing 5 grams of cacodyl chloride, 90 grams of formic acid, and 8 grams of alcohol; its specific gravity was 1.08. An anode solution of the same specific gravity was prepared from sulphuric acid. After sufficient anode solution and 11 cc. of cathode solution were run into the reduction cell and all the parts of the apparatus were adjusted, a current of 5 to 6 volts and 0.5 to 0.6 ampere was turned on. The cathode solution clouded almost immediately and after 500

[1] Ber. d. chem. Ges., **27**, 1378.
[2] This Journal, **35**, 3.

cc. of electrolytic hydrogen had been evolved in the voltameter, a heavy oil was found to have separated in the cell and a spontaneously inflammable gas *began* to be evolved with the cathode hydrogen—this gas increased in concentration during the remainder of the reduction. The oil, insoluble in formic acid, was identified as cacodyl; the gas was found to be dimethylarsine; hence the above equations are established.

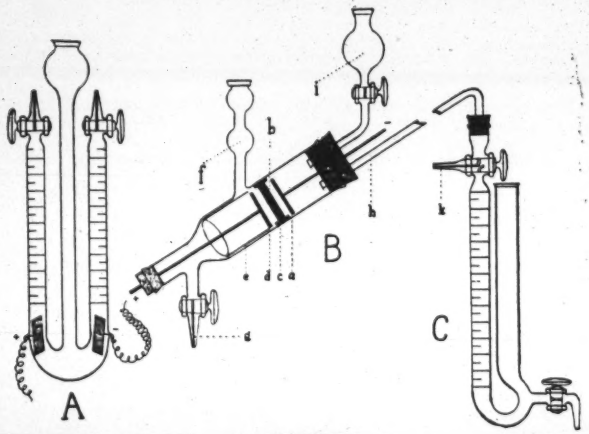


Fig. III.

A. A Hofmann U-tube placed in series with the cell and used as a hydrogen voltameter.
B. The reduction cell, made of glass.
C. Apparatus used to measure the gas evolved at the cathode and subsequently to deliver into Hempel burettes (at point *k*).

The following experiment was undertaken for the purpose of determining the relative rates of reduction of cacodyl chloride to cacodyl, and of the latter to dimethylarsine:

The cathode solution was prepared by dissolving 9.1 grams of cacodyl chloride in a mixture of 90 cc. of alcohol and 25 cc. of hydrochloric acid (sp. gr. 1.2); one fifth of this solution and a current of 5 to 6 volts and 1.05 to 1.20 amperes were used for the reduction. When exactly 50 cc. of hydrogen had

been evolved in the voltameter (II.), the current was turned off and the volume of mixed gases (III.) evolved from the cathode solution was measured in the apparatus C; the gas was next drawn over into a Hempel burette containing silver nitrate solution and, after shaking, the volume of the residual gas (unfixed hydrogen) was measured (V.) The loss in volume at this point represented an equivalent volume of dimethylarsine gas and one half of this volume was equivalent to the volume of hydrogen fixed by dimethylarsine. Fifty cc. of hydrogen, minus the volume of unfixed residual hydrogen and the hydrogen fixed by dimethylarsine, represented the volume of hydrogen fixed by cacodyl, according to the equation

$$2(CH_3)_2AsCl + H_2 = [(CH_3)_2As]_2 + 2HCl.$$

Reduction of Cacodyl Chloride.

I. No. of experiment.	II. Total hydrogen.	III. Burette gas.	IV. 50 cc. minus burette gas.	V. Residual gas ($AgNO_3$).	VI. Dimethylarsine.	VII. Hydrogen fixed by $(CH_3)_2AsH$.	VIII. Hydrogen fixed by cacodyl.
1	50	2.5	47.5	2.5	0.0	0.0	47.5
2	100	5.1	44.9	5.0	0.1	0.0	45.0
3	150	7.9	42.1	7.9	0.0	0.0	42.1
4	200	11.9	38.1	11.8	0.1	0.1	38.1
5	250	15.9	34.1	15.7	0.2	0.1	34.2
6	300	20.4	29.6	19.7	0.7	0.3	30.0
7	350	25.0	25.0	24.2	0.8	0.4	25.4
8	400	30.4	19.6	29.3	1.1	0.6	20.1
9	450	36.3	13.7	34.3	2.0	1.0	14.7
10	500	41.3	8.7	38.9	2.4	1.2	9.9
11	550	44.5	5.5	40.5	4.0	2.0	7.5
12	600	45.3	4.7	39.6	5.7	2.9	7.5
13	650	47.5	2.5	40.4	7.1	3.6	6.0
14	700	48.6	1.4	41.2	7.4	3.7	5.1
15	750	50.1	—0.1	40.9	9.2	4.6	4.5
16	800	50.8	—0.8	40.7	10.1	5.1	4.2
17	850	52.2	—2.2	41.9	10.3	5.2	2.9
18	900	52.2	—2.2	42.2	10.0	5.0	2.8
19	950	52.4	—2.4	42.2	10.2	5.1	2.7
20	1000	52.2	—2.2	42.1	10.1	5.0	2.9
22	1100	52.0	—2.0	42.8	9.2	4.6	2.6
24	1200	51.0	—1.0	43.9	7.1	3.5	2.6
26	1300	50.9	—0.9	45.1	5.8	2.8	2.1
28	1400	51.0	—1.0	45.9	5.1	2.6	1.5
30	1500	51.5	—1.5	47.0	3.5	1.7	1.3
32	1600	50.7	—0.7	48.2	2.5	1.2	0.6
34	1700	50.1	—0.1	49.0	1.1	0.6	0.4

It may be observed in the table: that the volume of gases evolved from the cathode solution, at first, is much less than the volume of the voltameter hydrogen collected during the same interval of reduction; then, at about the middle of the series of reductions, it becomes equal to the voltameter hydrogen; during most of the remainder of the reductions, the cathode gas volume is greater than the voltameter hydrogen; but finally, it becomes just equal to it. When cacodyl alone is formed, the residual hydrogen must be less than the voltameter hydrogen, owing to the *fixing* of hydrogen (the product being hydrochloric acid), as shown in the above equation. When dimethylarsine alone is formed by the reaction,

$$(CH_3)_2As—As(CH_3)_2 + H_2 = 2(CH_3)_2AsH,$$

the total volume of gas evolved must be greater than the voltameter hydrogen—two volumes of arsine resulting from one volume of hydrogen. Therefore, when both cacodyl and dimethylarsine are being formed, the burette gas represents the algebraic sum of these two reductions; and, depending upon the proportion of the two products, may be less or greater than the voltameter hydrogen. With the cubic centimeters of "fixed" hydrogen as ordinates and the quantity of electricity, measured in 50 cc. of hydrogen, as abscissas, (1) the composite curve of reduction, (2) the dimethylarsine curve, and (3) the cacodyl curve may be plotted, as shown in Fig. IV.

It will be seen that when the composite curve of reduction crosses the base line, the quantity of arsine is just twice that of the cacodyl.

As plotted, the area included within the cacodyl and dimethylarsine curves represents the total quantity of *hydrogen fixed*; the area included between the base line and a parallel line at 50 cc. represents the total *electrolytic hydrogen*.

From a consideration of the above experiments it may be anticipated that when cacodyl itself is reduced, the *composite curve* of reduction becomes coincident with the dimethylarsine curve. This is confirmed by the following experiment. A cathode solution was prepared by dissolving 5 cc. of crude cacodyl

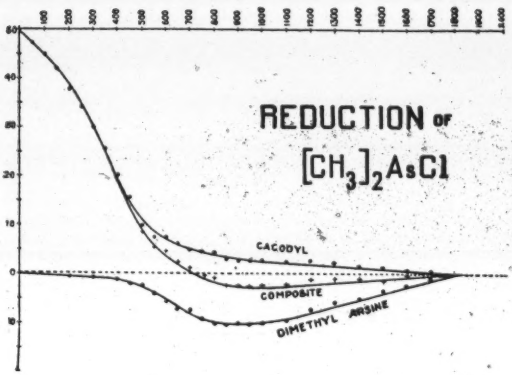


Fig. IV.

in a mixture of 50 cc. of alcohol and 25 cc. of hydrochloric acid (sp. gr. 1.20). With a current of 5 to 6 volts and 1.0 to 0.6 ampere, 20 cc. of this solution were reduced in the manner described above.

Reduction of Cacodyl.

I. Number of experiment.	II. Total hydrogen.	III. Burette gas.	IV. 50 cc. minus burette gas.	V. Residual gas ($AgNO_3$).	VI. Dimethyl-arsine.
1	50	36.0	14.0	36.0	0.0
2	100	37.4	12.6	37.3	0.1
3	150	38.9	11.1	38.5	0.4
4	200	40.3	9.7	39.6	0.7
5	250	41.8	8.2	41.1	0.7
6	300	43.6	6.4	42.6	1.0
7	350	46.2	3.8	44.8	1.4
8	400	47.6	2.4	45.7	1.9
9	450	49.1	0.9	46.6	2.5
10	500	50.4	—0.4	47.0	3.4
11	550	52.0	—2.0	48.0	4.0
12	600	52.8	—2.8	49.0	3.8
13	650	54.0	—4.0	49.0	5.0
14	700	55.0	—5.0	49.8	5.2
15	750	55.6	—5.6	50.1	5.5

Reduction of Cacodyl—(Continued).

I. Number of experiment.	II. Total hydrogen.	III. Burette gas.	IV. 50 cc. minus burette gas.	V. Residual gas ($AgNO_3$).	VI. Dimethylarsine.
16	800	55.9	—5.9	50.3	5.6
17	850	55.8	—5.8	50.3	5.5
18	900	55.7	—5.7	50.3	5.4
20	1000	55.1	—5.1	50.5	4.6
22	1100	53.9	—3.9	49.9	4.0
24	1200	52.8	—2.8	49.8	3.0
26	1300	51.8	—1.8	49.8	2.0
28	1400	50.8	—0.8	49.9	0.9
30	1500	50.2	+0.2	50.1	0.1

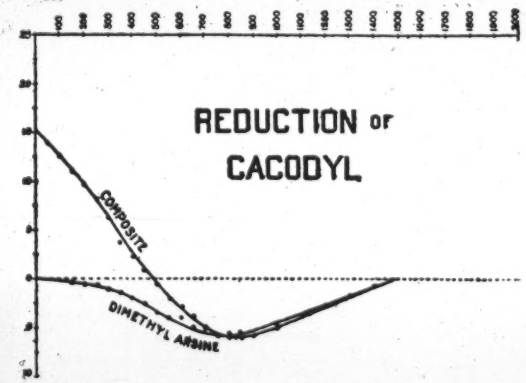


Fig. V.

That the burette readings were not immediately greater than the voltameter readings or, in other words, that the composite curve of reduction was not more nearly coincident with the dimethylarsine curve, is explained by the facts (1) that it is almost impossible to prepare and to handle pure cacodyl without its becoming oxidized, (2) crude cacodyl contains large quantities of cacodylic oxide, and (3) dimethylarsine is somewhat soluble in the above mentioned cathode

solution. However, the curves show sufficiently well that cacodyl is electrolytically reduced to dimethylarsine.

In view of the above experiments and since dimethylarsine is easily prepared from cacodylic acid by reduction with zinc and hydrochloric acid, it might be supposed that the electric current would induce the same reaction:

$$(CH_3)_2AsOOH + 4H = (CH_3)_2AsH + 2H_2O.$$

However, experiments showed that no arsine was evolved; an explanation of this is seen in the following equations:

$$(CH_3)_2AsO_2H = (CH_3)_2AsO_2^- + H^+,$$
$$2(CH_3)_2AsO_2 + H_2O = 2(CH_3)_2AsO_2H + O.$$

II. Primary Arsines.

With Elrick Williams.

Studies with Gaseous Primary Methylarsine.

The sodium salt of methylarsonic acid[1] was reduced by zinc and hydrochloric acid[2] and the mixture of hydrogen and gaseous methylarsine was passed into a large bottle filled with water and so arranged that the gaseous mixture could both be preserved free from oxidation and also so that portions of it, as desired, could be drawn off into Hempel burettes. Usually the gaseous mixture was drawn out by depressing the companion tube of the Hempel burette; then boiled water was permitted to run into the gas reservoir, so as to equalize the interior and exterior pressures. Samples of the gas in the Hempel tube were treated with solutions as indicated in the following table of preliminary experiments; from time to time the concentration of the arsine in the reservoir was determined by treatment with silver nitrate solution.[3]

[1] Ann. Chem. (Liebig), **249**, 147.
[2] This Journal, **33**, 120.
[3] *Ibid.*, **33**, 125.

Reactions of Monomethylarsine.

Exp. No.	Reagent, aqueous solution.	Volume of gas taken.	Volume loss resulting.	Per cent of loss.	Known per cent of arsine.	Time in minutes.	Observations and remarks.
1	$KMnO_4$	88.8	12.2	13.8	13.10	3–5	Brown black precipitate; odorless product; acid reaction.
2	$KMnO_4$	87.7	10.7	12.2	12.80	3–5	Precipitate lost 24.10 per cent on igniting.
3	$K_3Fe(CN)_6$	91.8	9.5	10.34	10.35	30	Sol. yellow; white precipitate; odor RAsO and HCN.
4	$FeCl_3$	86.0	8.7	10.10	10.20	30+	Sol. green; white precipitate; odor RAsO.
5	$Pb(Ac)_2$	86.3	5.9	6.80	6.60	60	Reaction slow; black precipitate; odorless.
6	$K_2Cr_2O_7$	92.0	9.8	10.60	10.35	10	Sol. darkened; product odorless.
7	H_2CrO_4	96.0	20.4	21.25	21.20	2–3	Same as Exp. 6.
8	H_2O_2	93.3	2.9	3.10	10.35	60	O_2 evolved; cloudy sol.; $\frac{1}{2}RAsH_2$ remained.
9	Br_2	92.4	9.6	10.60	10.35	1–2	*White solid*; then clear, odorless solution.
10	$HgCl_2$	87.0	9.3	10.70	10.35	1–2	White; *then silky, golden solid*; brown red; darker.
11	$CuSO_4$	86.9	7.0	8.05	9.02	1–2	Blueness lost; *red brown, silky solid* formed.
12	HNO_3	92.4	9.5	10.29	10.35	3–5	NO and $RAsO_3H_2$ formed.
13	conc. H_2SO_4	72.1	11.4	15.81	19.17	1–2	Light yellow solid; SO_2 but no H_2S.
14	conc. HNO_3	95.1	15.9	16.72	21.20	1–2	N_2 or N_2O formed; RAsO and $RAsO_3H_2$.
15	$SbCl_3$	77.8	5.8	7.15	7.50	1–2	*Silky, white solid*; then yellow; finally amorphous; red.
16	$AsCl_3$	92.4	21.0	22.70	21.20	3–5	Residual gas free from arsenic.
17	KdCl	93.6	19.7	21.05	21.20	30	Residual gas fumed.
18	Kd-Kd	77.8	17.2	21.11	21.20	30	Fumed, of course.
19	$SnCl_4$	93.0	19.9	21.40	21.20	3–5	*Yellow white solid*; yellow oil; residual gas contained arsenic.
20	PCl_3	61.2	8.2	13.40	13.75	5	Orange solid; residual gas free from arsenic.
21	S_2Cl_2	98.4	19.8	20.12	21.20	5	Yellow cheeselike solid; residual gas contained S.
22	SO_2	71.8	4.8	6.69	7.00	60	Opaque sol.; no H_2S in residual gas.
23	PbO_2	81.5	14.0	17.19	21.20	4000	Red brown solid; filtered sol. contained Pb.

Interpretations of the above data render probable the following equations:

1. $6KMnO_4 + 5RAsH_2 = 6MnO + 3RAsO_3K_2 + 2RAsO_3H_2 + 3H_2O.$
2. $6KMnO_4 + 5RAsH_2 = 4MnO + 3RAsO_3K_2 + 2RAsO_3Mn + 5H_2O.$
3. $4K_3Fe(CN)_6 + RAsH_2 + H_2O = 3K_4Fe(CN)_6 + H_4Fe(CN)_6 + RAsO.$[1]
4. $4FeCl_3 + RAsH_2 + H_2O = 4FeCl_2 + 4HCl + RAsO.$[2]
5. $4Pb(AC)_2 + RAsH_2 + 3H_2O = 3Pb + 8HC_2H_3O_2 + RAsO_3Pb.$[2]
6. $K_2Cr_2O_7 + RAsH_2 =$ (See THIS JOURNAL, **35**, 28).
7. $6H_2CrO_4 + 2RAsH_2 = 3(2CrO_2.H_2O) + 2RAsO_3H_2 + 3H_2O.$[3]
8. $2H_2O_2 + RAsH_2 = RAsO + 3H_2O.$
9. $3Br_2 + RAsH_2 + 3H_2O = RAsO_3H_2 + 6HBr.$[4]
10. $HgCl_2 + RAsH_2 =$ RAsHHgCl.HCl (etc.).[5]
11. $CuSO_4 + RAsH_2 =$ $RAsH_2.CuSO_4$(?),
12. $6HNO_2 + RAsH_2 = RAsO_3H_2 + 6NO + 3H_2O.$[6]
13. $H_2SO_4 + RAsH_2 = RAsH_2.H_2SO_4.$[7]
14. $HNO_3 + RAsH_2 =$ (See THIS JOURNAL, **33**, 125; **35**, 27).
15. $SbCl_3 + RAsH_2 =$ (See page 112).
16. $AsCl_3 + RAsH_2 =$ See page 111).
17. $(CH_3)_2AsCl + RAsH_2 =$ (See page 122).
18. $(CH_3)_2AsAs(CH_3)_2 + RAsH_2 =$ No reaction.
19. $SnCl_4 + RAsH_2 =$ (See page 110).
20. $PCl_3 + RAsH_2 =$ (See page 111).
21. $S_2Cl_2 + RAsH_2 = RAsCl_2 + S + H_2S.$[8]
22. $SO_2 + RAsH_2 =$ (See THIS JOURNAL, **35**, 38).
23. $PbO_2 + RAsH_2 =$ (See THIS JOURNAL, **35**, 30).

[1] Cf. THIS JOURNAL **35**, 35.
[2] *Ibid.*, **35**, 30.
[3] *Ibid.*, **35**, 28.
[4] *Ibid.*, **33**, 126; **35**, 14.
[5] *Ibid.*, **33**, 127; **35**, 35.
[6] *Ibid.*, **35**, 26.
[7] *Ibid.*, **35**, 24.
[8] *Ibid.*, **35**, 39.

Monomethylarsine and Gases.

Exp. No.	Gas.	Volume of gas.	Volume $RAsH_2$ mixture.	Volume of contained $RAsH_2$.	Volume loss.	Ratio loss to $RAsH_2$.	Time. Min.	Observations and remarks.
1	O_2	24.3	60.7	4.4	11.0	2.5	30	White solid; then brick red with white.
2	O_2	32.4	64.0	4.6	10.2	2.3	30	Shaking 20 minutes—loss 2.2 cc.; letting stand 1 minute—loss 3 cc. more; water retards oxidation.
3	N_2O	29.7	62.6	4.5	0.2		30	Residual gas yielded $RAsH_2$.
4	NO	50.1	61.0	4.4	1.0		30	Residual gas showed NO and $RAsH_2$.
5	NO_2	30.5	47.3	3.1	6.3	2.0	5	Residual gas showed NO but no $RAsH_2$.

These reactions are probably represented by the following equations:

1. $3O_2 + 2RAsH_2 = 2RAsO_3H_2$ (ratio 2.5 : 1).
   $2O_2 + 4RAsH_2 = (RAs)_4 + 4H_2O$ (ratio 1.5 : 1) [1]
2. $O_2 + RAsH_2 = RAsO + H_2O$ (ratio 1 : 1).
3. $N_2O + RAsH_2 =$ no reaction.[2]
4. $NO + RAsH_2 =$ no reaction.[3]
5. $3NO_2 + RAsH_2 = 3NO + RAsO_3H_2$.

[1] See THIS JOURNAL, **35**, 9.
[2] *Ibid.*, **35**, 25.
[3] *Ibid.*, **35**, 26.

Hydriodic Acid and Methylarsine.—A mixture of 50.4 cc. of gaseous methylarsine (8.1 cc.) and hydrogen (42.3 cc.), treated over mercury with 1 cc. of concentrated aqueous hydriodic acid, *increased* 2 cc. in volume in 20 minutes; after heating for 20 minutes more at 100°, an increase of 10.9 cc. in volume resulted. The gaseous mixture, after cooling to the original temperature, was treated with a solution of silver nitrate—a decrease in volume of 6.7 cc. resulted. From these experiments it is concluded that the following reactions are slow[1] or are easily reversible:

$$CH_3AsH_2 + HI \rightleftarrows CH_3AsH_3I \longrightarrow CH_3AsHI + H_2,$$
$$CH_3AsHI + HI \rightleftarrows CH_3AsH_2I_2 \longrightarrow CH_3AsI_2 + H_2.$$

Propyl Iodide and Methylarsine.—When a gaseous mixture of 75.5 cc. of methylarsine (10.1 cc.) and hydrogen (63.4 cc.), with 1 cc. of liquid *n*-propyl iodide, was heated for one hour at 100° in a mercury eudiometer, a decrease in volume of 4 cc. was observed on cooling to the original temperature. When treated with silver nitrate solution, the residual gas suffered a loss of 5.8 cc. (unchanged methylarsine). During the experiment, *light yellow crystals* (melting below 100°) were observed on the walls of the eudiometer; therefore the following equation is justified:[2]

$$CH_3AsH_2 + C_3H_7I \rightleftarrows (CH_3)(C_3H_7)AsH_2I.$$

Silver Nitrate and Methylarsine.[3]—The black precipitate in a gas burette, after treatment of a silver nitrate solution with quantities of methylarsine, was washed with water and dried at 100°.

0.5439 gram of substance gave 0.4430 gram of AgCl.

	Calculated for $CH_3AsO_3Ag_2$.	Found.
Ag	60.69	79.90

Since methylarsonic acid was found in the precipitate, the latter is evidently a mixture of metallic silver and silver methylarsonate.

[1] Cf. THIS JOURNAL, **35**, 27.

[2] Addition products are almost invariably observed when primary, secondary, and tertiary arsines are treated with alkyl iodides. Cf. THIS JOURNAL, **33**, 128, and see pages 121, 122, and 123.

[3] Cf. THIS JOURNAL, **33**, 126; **35**, 35.

Methylarsine Oxide and Methylarsine.—When the white methylarsine oxide, formed on the walls of a Hempel burette by the reaction of atmospheric oxygen with methylarsine, was treated with gaseous methylarsine, all of the methylarsine was fixed and a brick red solid replaced the white oxide. Evidently the following reaction:

$$2CH_3AsO + 2CH_3AsH_2 \longrightarrow (CH_3As)_4 + 2H_2O;$$

explains the formation of the red polymers always formed by the spontaneous oxidation of the arsines. The details of the reaction are shown as follows:

$$\begin{array}{l} CH_3{-}As{=}O \\ \quad\vdots\vdots \\ CH_3{-}As{=}H_2 \end{array} \longrightarrow \begin{array}{l} CH_3{-}As{-}OH \\ \quad\vert \\ CH_3{-}As{-}H \end{array} \longrightarrow \begin{array}{l} CH_3{-}As \\ \quad\vert \\ CH_3{-}As \end{array} + H_2O;$$

two groups, $CH_3{-}As{-}As{-}CH_3$, condensing and evidently forming $\begin{array}{l} CH_3{-}As{-}As{-}CH_3 \\ \quad\vert\quad\vert \\ CH_3{-}As{-}As{-}CH_3 \end{array}$.

The following substances failed to react with gaseous methylarsine: hydrogen sulphide, yellow ammonium sulphide, potassium nitrite, potassium hydroxide, nickelous chloride, formaldehyde, acetic acid, aniline, nitrobenzene, and benzotrichloride.

Reactions of Ethylarsine.

Iodine.—When equimolecular quantities of the two substances were brought together in a sealed tube containing ether, the color of the iodine was quickly discharged and a golden yellow solution resulted. Hydrogen and an oil boiling at 205° to 210° and containing 63.8 per cent of iodine (calculated for $C_2H_5AsI_2$[1] is 70.9 per cent) were obtained. The following equation is justified:

$$C_2H_5AsH_2 + I_2 = C_2H_5AsI_2 + H_2.$$

Bromine.—When equimolecular quantities of ethylarsine and bromine were brought together in ether, a *red brown, amorphous solid* was formed immediately and remained permanently (one year) undissolved. Considerable pressure (hydrogen)

[1] Ann. Chem. (Liebig), 118, 367.

was observed on opening the tube; the ether solution yielded, by distillation, an oil, *ethylarsine dibromide*, boiling at 192°.

0.4120 gram substance gave 0.5812 gram AgBr.

	Calculated for $C_2H_5AsBr_2$.	Found.
Br	60.60	60.03

When treated with platinic chloride the dibromide liberated heat and slowly formed yellow white crystals, which were dried on the water bath and ignited.

0.8622 gram substance gave 0.2700 gram Pt.

	Calculated for $C_2H_5AsBr_2.PtCl_4$.[1]	Found.
Pt	32.68	31.31

The brown residue from the sealed tube experiment was analyzed:

0.1865 gram substance gave 0.0260 gram AgBr.

0.2106 " " " 0.2247 gram $Mg_2As_2O_7$.

	Calculated for		Found.
	$(C_2H_5As)_4$.	C_2H_5AsHBr.	
Br	0.00	43.24	10.25
As	72.11	40.54	51.62

Evidently this substance is a mixture. The end reaction of the arsine with bromine is as follows:

$$C_2H_5AsH_2 + Br_2 = C_2H_5AsBr_2 + H_2;$$

while positive evidence of intermediate products is deduced.

Sulphur.—When 2 grams of ethylarsine (1 mol.) and 1.2 grams of sulphur (2 atoms) were brought together in a sealed tube filled with carbon dioxide, the sulphur was seen to dissolve rapidly, and to yield a viscid, colorless liquid. On opening the tube, great pressure (hydrogen sulphide, but no hydrogen) was observed. The percentage of sulphur in the gluelike mass was determined:

0.1962 gram substance gave 0.3475 gram $BaSO_4$.

	Calculated for		Found.
	$C_2H_5AsS_2$.	C_2H_5AsS.	
S	38.09	23.52	24.28

[1] Cf. THIS JOURNAL, **35**, 32.

Evidently the substance is *ethylarsine sulphide* with an admixture of free sulphur or the disulphide, and the original reaction is as follows:

$$C_2H_5AsH_2 + S_2 = C_2H_5AsS + H_2S.$$

Mercuric Chloride.—When equimolecular quantities of the two substances were brought together in a sealed tube filled with carbon dioxide, a dark *yellow black precipitate* formed immediately and changed after a time to a compact, finely divided, black precipitate. On opening the tube no hydrogen or mercurous chloride, but gaseous hydrochloric acid and metallic mercury were found. An ether solution of the oil became yellow red in the air and ethylarsine dichloride was detected in the ether solution, therefore the final reaction is expressed by the following equation:[1]

$$C_2H_5AsH_2 + 2HgCl_2 = C_2H_5AsCl_2 + 2Hg + 2HCl.$$

Mercuric Iodide.—When 2.5 grams of ethylarsine (1 mol.) and 10.7 grams of mercuric iodide (1 mol.) were brought together in ether contained in a sealed tube, a *bright yellow product* was formed immediately. On opening the tube hydrogen, mercurous iodide (4 grams—calculated, 7.7 grams), and an oil (5.7 grams) were obtained; the oil showed the presence of ethylarsine diiodide, therefore the reaction here is as follows:

$$C_2H_5AsH_2 + 2HgI_2 = C_2H_5AsI_2 + 2HgI + H_2.$$

Stannic Chloride.—When 2.14 grams of ethylarsine (1 mol.) and 5.9 grams of stannic chloride (1 mol.) were sealed with ether in a tube, no solid formed even after standing for 14 months. No pressure was observed on opening the tube; the greenish yellow solution was concentrated and then treated with water; the aqueous solution contained the Sn″ ion and the oil separating was found to distil at 156° (ethylarsine dichloride boils at 156°).[2] The formation of the end products is explained by the equation

$$C_2H_5AsH_2 + 2SnCl_4 = C_2H_5AsCl_2 + 2SnCl_2 + 2HCl,$$

[1] See page 104, and cf. THIS JOURNAL, **33**, 127; **35**, 35.
[2] La Coste: Ann. Chem. (Liebig), **208**, 33.

though evidence of intermediate products[1] was manifest in the oil separated.

Phosphorus Trichloride.—When equimolecular quantities of the two substances were brought together in an ether solution contained in a sealed tube, *a fine yellow powder* separated slowly. After 14 months the tube was opened; gaseous hydrochloric acid, ethylarsine dichloride, and a yellow orange solid were obtained. The residue persisted in giving off the odor of ethylarsine dichloride even though washed repeatedly with ether; the main ether solution, on being shaken with solid calcium chloride, gave a voluminous precipitate of a red brown substance. Evidently there was in solution some substance other than the *free* original compounds or the end product, ethylarsine dichloride.

Arsenic Trichloride.—When equimolecular quantities of the two substances were brought together in a sealed tube containing ether, *a yellow solid* appeared and changed rapidly to a curdy, *brick red* solid. Ethylarsine dichloride was found in the ether solution; the residue was analyzed for arsenic:

0.1387 gram substance gave 0.2214 gram $Mg_2As_2O_7$.

	Calculated for $(C_2H_5As)x$.	Found.
As	72.11	77.24

Evidently this residue is a mixture of the polymer $(C_2H_5As)_x$ with metallic arsenic and the equation representing the reaction is

$$8C_2H_5AsH_2 + 8AsCl_3 = (C_2H_5As)_4 + 4C_2H_5AsCl_2 + 16HCl + 8As.$$[2]

Antimony Trichloride.—When equimolecular quantities of the two substances were brought together in a sealed tube containing ether, a *red brown, amorphous solid* was formed immediately, but in the course of 14 months it changed to a *jet black solid*. Considerable pressure of gaseous hydrochloric acid was observed on opening the tube. The ether solution yielded ethylarsine dichloride and a little unchanged antimony trichloride; the black residue was washed repeatedly with ether but,

[1] Cf. THIS JOURNAL, **38**, 39.

[2] Cf page 126.

on drying, *inflamed spontaneously.* Unquestionably intermediate products were formed in this experiment.

Water.—When 2 grams of ethylarsine and 5 grams of water were heated in a sealed tube for six hours at 180°, no evidence of a reaction could be observed.

Hydrochloric Acid Solution.—When ethylarsine was treated with an excess of one molecule of hydrochloric acid (sp. gr. 1.20) and the mixture was heated for two hours at 70°, no evidence of a reaction could be observed.

Isopropyl Iodide and Ethylarsine.—When 3.7 grams of ethylarsine and 18 grams of isopropyl iodide were heated to 70° for one hour in a sealed tube filled with carbon dioxide, no condensation was observed; after heating for three hours at 110°, a dark, red brown oil was obtained. The arsonium iodide (90 per cent) was separated in the usual manner; 0.2450 gram required 0.1155 gram of $AgNO_3$ = 35.22 per cent iodine; calculated, 35.18 per cent.

When a sample of 0.0546 gram of the *triisopropylethylarsonium iodide* was heated in the tensimeter molecular weight apparatus[1] the following data were obtained:

t.	Vapor pressure.	Vapor volume.	Apparent mol. wt.	Theoretical mol. wt.
130	0.0	0.0	.....	360
179	1.2	0.007	.....	...
198	8.3	0.044	.....	...
234	388.3	2.066	411.6	...
240	1092.0	2.578	279.0	...
262	2138.0	3.428	146 5	...

The volume of nonreversible vapor at 28° was 2.7 cc.; it burned with a luminous flame, was free from arsenic and iodine, and was not affected by bromine water. On cooling, the residue, possessing an odor of tertiary arsine, consisted of a red yellow oil and light yellow crystals; the product reacted strongly with bromine water. Evidently triisopropylethylarsonium iodide *decomposes at its melting point,* according to the following reactions:

$$(C_3H_7)_3(C_2H_5)AsI = (C_3H_7)_3As + C_2H_5I,$$
$$2(C_3H_7)_3C_2H_5AsI = (C_3H_7)_3AsI_2 + C_4H_{10} + (C_3H_7)_3As.$$

[1] J. Am. Chem. Soc., **29**, 1052.

n-Propyl Iodide and Ethylarsine.—When 2 grams of ethylarsine and 10 grams of *n*-propyl iodide were sealed in tubes filled with carbon dioxide and heated for one hour at 70°, no effect was observed; heated for three hours at 110°, much pressure (hydrogen) and a red oil were observed. *Tri-n-propylethylarsonium iodide* was separated and found to soften at 230° and melt at 237°, with decomposition. An alcoholic solution of the iodide treated with an alcoholic solution of mercuric iodide gave a light, yellow white precipitate, which, after recrystallizing from alcohol, gave, on analysis, 22.09 per cent of iodine; calculated for $(C_2H_5)(C_3H_7)_3AsHgI$ = 22.64 per cent.[1]

Propylarsine.

n-Propylarsonic acid[2] (95 grams) and amalgamated zinc dust (500 grams) were placed in a flask and treated with concentrated hydrochloric acid, in the usual manner;[3] the *propylarsine* was condensed in a sulphur dioxide condenser surrounded by a freezing mixture. After transferring to bulbs of the proper size, it was analyzed:

0.1603 gram substance gave 0.1724 gram CO_2 and 0.1088 gram H_2O.

	Calculated for $C_3H_7AsH_2$.	Found.
C	7.50	7.54
H	30.00	29.33

Monobenzylarsine.

A 2-liter, hard glass, round bottom flask, containing 52 grams of benzylarsonic acid,[4] 200 cc. of ether, and 500 grams of amalgamated zinc dust[5] was connected with a reflux condenser, a dropping funnel, and a mercury valve; concentrated hydrochloric acid was dropped in until the reduction was complete:

$$C_6H_5CH_2AsO_3H_2 + 6H = C_6H_5CH_2AsH_2 + 3H_2O.$$

As the reduction proceeded, some red oxidation product was deposited upon the inner walls of the flask and a distinct odor

[1] Cf. Ann. Chem. (Liebig), **341**, 182.
[2] J. Am. Chem. Soc., **28**, 352.
[3] This Journal, **33**, 120; **35**, 3.
[4] J. Am. Chem. Soc., **28**, 354.
[5] This Journal, **33**, 118.

of arsine was observed. After 2 to 3 days, more ether was added and the flask was shaken, then water was admitted through the dropping funnel until all of the ether solution (somewhat green in color) was forced up into a separatory funnel containing sticks of calcium chloride and filled with carbon dioxide. The separatory funnel was closed and shaken until the ether solution was dried. A Brühl distilling apparatus, properly connected with a condenser, a flask, and an inverted U-shaped delivery tube, was partially exhausted by means of the water pump; the delivery tube with proper connections was dipped to the bottom of the ether solution contained in the separatory funnel and the distilling flask was about half filled with the ether solution. By means of the pump, the ether solution was soon concentrated, then more of it was drawn in; this process was repeated until all of the ether solution had been evaporated at room temperature. The residual liquid, light yellow in color, was distilled, and the following fractions were obtained:

1.	140°	262 mm.	8.5 grams
2.	140°	260 "	4.1 "
3.	141°	260 "	3.2 "

The residue in the distilling flask changed finally and rather abruptly to a dark red solid. The apparatus was then filled with carbon dioxide and small bulbs, containing carbon dioxide, were filled with the different fractions:

0.1236 gram of fraction (1) gave 0.2260 gram CO_2 and 0.0602 gram H_2O.

	Calculated for $C_7H_9AsH_2$.	Found.
C	50.00	49.87
H	5.35	5.41

Benzylarsine is a faintly yellow liquid boiling at 140° under 262 mm. pressure.

Benzylarsine and Platinic Chloride.—When equimolecular weights of benzylarsine and platinic chloride (10 per cent solution) were brought together in a sealed tube, a black, oily substance, followed by a black amorphous mass, was noticed. After being washed with alcohol and ether, the *chlorplatinate*

was dried and ignited; the odors of arsenic trioxide and stibine were given off during the heating.

0.1121 gram substance yielded 0.0423 gram Pt.

	Calculated for $C_7H_7AsH_2.PtCl_4$.	Found.
Pt	38.49	38.18

Hydriodic Acid.—Heated with 2 molecules of hydriodic acid at 140° for one hour, the benzylarsine yielded hydrogen, a brown black solid,[1] and an oil (evidently benzylarsine diiodide).

Bromine.—With a molecule of bromine at ordinary temperature, the arsine yielded hydrogen, *transparent crystals*, and a heavy, dark oil.

Oxygen.—Permitted to oxidize in the air, the arsine yielded benzylarsonic acid (melting at 167°) and a red product, which was analyzed:

0.1180 gram substance gave 0.1837 gram $Mg_2As_2O_7$.

	Calculated for $(C_7H_7As)_4$.	Found.
As	76.72	75.33

Tripropylarsine.

When 103 grams of *n*-propyl chloride, 120 grams of arsenic trichloride, and 75 grams of sodium were brought together in a flask attached to a long reflux condenser, a reaction took place;[2] after standing all night and heating gently for 1 to 2 hours on the water bath, the reaction was found to be complete. After filtering rapidly and distilling off the ether, 60 grams of oil were obtained; this was distilled three times at ordinary pressure and the following fractions were obtained:

1.	100°–140°	2 grams	4.	205°–220°	10 grams
2.	140°–200°	8 "	5.	220°–270°	4 "
3.	200°–205°	18 "			

The lower fractions showed the presence of 2 to 3 per cent of chlorine; evidently primary and secondary arsine chlorides were present; on standing exposed to the air, a white solid formed and the oil separated into two layers; the solid gave, on

[1] See page 120.

[2] Cf. THIS JOURNAL, **38**, 42.

analysis, 4 per cent of chlorine; evidently the compound $(C_3H_7)_3AsO.(C_3H_7)_2AsOCl$ was formed.

The fractions below 210° were boiled with an excess of bromine water; after concentrating, the heavy, red oil (25 grams) was washed with water, dried, and analyzed for bromine (21.42 per cent Br, calculated for $(C_3H_7)_3AsBr_2$ = 43.90 per cent). To remove the primary and secondary arsine derivatives which evidently were present, the oil was heated with aqueous ammonia and the residual oil was removed, reduced by means of zinc and hydrochloric acid, extracted with ether, and distilled under reduced pressure. It boiled at 167° (90 mm.) and 158° (73 mm.).

0.1312 gram substance gave 0.2550 gram CO_2 and 0.1183 gram H_2O.

	Calculated for $(C_3H_7)_3As$.	Found.
C	52.94	53.02
H	9.95	10.02

A molecular weight determination by the Dehn method[1] was made: 0.2242 gram substance gave 12.99 cc. of vapor at 1564 mm. and above 251°. Vapor pressures: 92°—161 mm.; 143°—283 mm.; 195°—482 mm.; 212°—844 mm.; 251°—1564 mm.

	Calculated for $(C_3H_7)_3As$.	Found.
Mol. wt.	202	204

Oxygen.—When tripropylarsine was brought into contact with air contained in the Dehn hygrometer,[2] no change in volume was observed; when a little concentrated sulphuric acid was then admitted, rapid oxidation resulted, as was shown by the rapid decrease of the air volume.

Decomposition of Arsenic Derivatives by Heat.[3]

Isoamylarsonic Acid.[4]—When 7.2 grams of the pure acid were heated in a sealed tube filled with carbon dioxide, no reaction was noticeable even after heating for 15 hours at 180° (the acid

[1] J. Am. Chem. Soc., **29**, 1063.
[2] *Ibid.*, **29**, 1053.
[3] Cf. J. Am. Chem. Soc., **28**, 355–59; THIS JOURNAL, **35**, 8.
[4] J. Am. Chem. Soc., **28**, 353.

melts at 194°). After heating for three hours at 240°, a slight darkening and a partial yield of a liquid were observed; after heating for four hours at 285°, the formation of the liquid and a mass of pearly crystals was complete. On opening the tube, no pressure was observed; on distilling the liquid contents, a large yield of isoamyl alcohol and some isoamyl oxide was obtained. Since the flat, pearly crystals did not melt at 300°, did not suffer a loss in weight on subliming, and when dissolved in hydrochloric acid yielded with hydrogen sulphide a yellow precipitate, they were identified as arsenic trioxide. Therefore the above decomposition was as follows:

$$2C_5H_{11}AsO_3H_2 = 2C_5H_{11}OH + As_2O_3 + H_2O.$$

Phenylarsonic Acid.[1]—This acid did not decompose on heating for three hours at 285° (melting point, 158°); after heating for twenty-four hours at 320° it was changed to two liquid layers and a white solid (arsenic trioxide). The upper, dark colored liquid layer was separated from the lower layer (water) and identified as phenyl oxide (boiling point, 252°), therefore we have the following reaction:

$$2C_6H_5AsO_3H_2 = (C_6H_5)_2O + As_2O_3 + 2H_2O.$$

Monophenylarsine.[2]—When this compound was sealed in a tube with carbon dioxide and heated for two hours at 180°, no change was observed on cooling; after heating for three hours at 240°, a red brown solid and a light green oil were found; after heating for three hours more at 310°, a black residue coating the inner surfaces of the tube was observed. The excess of gas found in the tube proved to be hydrogen; an ether extract of the residue yielded well-defined crystals of triphenylarsine; the black residue contained 95.1 per cent of arsenic. Therefore the reaction is expressed by the following equation:

$$3C_6H_5AsH_2 = (C_6H_5)_3As + 2As + 3H_2.$$

Monomethylarsine.[3]—This primary arsine was heated for three hours at 240° without effect; after heating for three

[1] Ann. Chem. (Liebig), **208**, 34; THIS JOURNAL, **33**, 132.
[2] THIS JOURNAL, **33**, 147.
[3] Ber. d. chem. Ges., **34**, 3597. THIS JOURNAL, **33**, 120.

hours at 310° it yielded a black, metallic mirror. The excess of gas formed was washed successively with solutions of sodium hydroxide, silver nitrate, and bromine; the residual gas, which burned with a blue flame, was proved by the explosion method to be a mixture of methane and hydrogen. At least one phase of the decomposition is expressed by the equation

$$2CH_3AsH_2 = 2CH_4 + 2As + H_2.$$

Monoethylarsine.[1]—When this arsine was heated for three hours at 210°, only a slight blackening was noticed; after three hours at 235°, the black metallic deposit on the walls of the tube was complete. The excess of gas in the tube was washed as described above. On exploding 0.9 of the residual gas in the presence of an excess of oxygen, it suffered a loss of 11.3 cc.; with potassium hydroxide a further loss of 8.4 cc. resulted. The black deposit (0.1036 gram) yielded 95.17 per cent of arsenic (0.1990 gram $Mg_2As_2O_7$). An alcohol-ether extract of the original contents of the tube yielded some triethylarsine. Therefore the following reactions are involved:

$$2C_2H_5AsH_2 = 2C_2H_6 + 2As + H_2,$$
$$3C_2H_5AsH_2 = (C_2H_5)_3As + 2As + 3H_2.$$

Diisoamylarsine.[2]—Heating for two hours at 220° yielded a little red solid; heating for three hours at 240° to 260° gave a black, metallic deposit. When 65 cc. of the excess gas were freed from carbon dioxide (22.2 cc.) and then was treated with bromine water, a contraction of 2.0 cc. resulted; the residual gas burned with a luminous flame. The liquid contents of the tube, after extracting with alcohol and ether, yielded at about 175° a liquid burning without depositing arsenic (decane) and at about 240° a liquid which, by its odor, by its decomposition on heating, and by its reaction with bromine, was proved to be *triisoamylarsine*. The black solid (0.1407 gram) gave on one analysis 86.48 per cent of arsenic (0.2466 gram $Mg_2As_2O_7$). The consecutive reactions probably are as follows:

$$6(C_5H_{11})_2AsH = 4(C_5H_{11})_3As + 2As + 3H_2,$$
$$2(C_5H_{11})_2AsH = C_5H_{10} + C_5H_{12} + C_{10}H_{22} + 2As.$$

[1] THIS JOURNAL, **33**, 143.
[2] *Ibid.*, **35**, 53.

Diphenylarsine.[1]—Heating for two hours at 245° produced only a little blackening; heating for three hours at 295° effected decomposition. The residual excess gas proved to be hydrogen; the alcohol-ether extract of the residue yielded a white, crystalline product, which (0.0852 gram) yielded on analysis 25.15 per cent of arsenic (0.0443 gram $Mg_2As_2O_7$)—evidently it was triphenylarsine (calculated, As = 24.51 per cent). Two analyses of the black residue (77.46 per cent As and 77.70 per cent As) showed here, as in other cases of its production, that it is probably mixed with the tertiary arsine. The reactions are expressed by the following equations:

$$6(C_6H_5)_2AsH = 4(C_6H_5)_3As + 2As + 3H_2,$$
$$2(C_6H_5)_3As = 3C_{12}H_{10} + 2As.$$

Tripropylarsine.[2]—No evidence of decomposition was noticeable below 287°; after heating for two hours at 295°, a yellow liquid was observed. On opening the tube considerable pressure was noticed; 44 cc. of this gas, after washing successively with caustic soda and bromine water, gave 16 cc. of gas which by shaking with alcohol lost 8.5 cc. The gas which was soluble in alcohol burned with a blue flame. The residual liquid in the tube had a cacodyllike odor. The probable partial reaction was

$$4(C_3H_7)_3As = (C_3H_7As)_4 + 4C_6H_{14}.$$

Triethylarsine.—Heated at 190° to 215° for three hours, it darkened; at 245° for two hours, a yellow oil and some solid were formed; at 265° for three hours, considerable excess gas, a greenish yellow to gray black residue and only a little liquid were observed. The solid gave, on analysis, 44.09 per cent arsenic (0.1264 gram gave 0.1129 gram $Mg_2As_2O_7$); calculated for $(C_2H_5)_3As$ = 46.29. The alcohol-ether extract of the solid yielded an oil which by its odor and reaction with bromine was shown to be unchanged triethylarsine. The probable partial reaction was

$$4(C_2H_5)_3As = (C_2H_5As)_4 + 4C_4H_{10}.$$

[1] THIS JOURNAL, **38**, 45.
[2] See page 115.

Benzylarsine.[1]—When 0.5 gram of benzylarsine, in a sealed tube from which the air had been exhausted, was heated for two hours at 250°, a reaction resulted. A little gas, a little oil, and a glistening, black solid were formed. The black solid was washed and analyzed; 0.1473 gram gave 0.1370 gram $Mg_2As_2O_7$, which is equivalent to 45.00 per cent of arsenic—calculated for $(C_6H_5CH_2As)_4$ is 45.18 per cent. Therefore the following reaction probably takes place:

$$4C_6H_5CH_2AsH_2 \longrightarrow (C_6H_5CH_2As)_4 + 4H_2.$$

Cacodyl.[2]—When 5.3 grams of crude cacodyl (cacodylic oxide) were heated for two hours at 340° in a sealed tube filled with carbon dioxide, a black, metallic deposit and a mobile, yellow oil were formed; on opening the tube considerable pressure was observed. After washing with a solution of potash, the residual gas (about 25 per cent) was found to burn with an arsenic flame and to dissolve in a solution of silver nitrate; its odor and other properties characterized it as trimethylarsine.[3] After freeing it from the oil and washing it with alcohol and ether, 0.1446 gram of the black residue yielded 0.2500 gram $Mg_2As_2O_7$ or 83.65 per cent As; calculated for $(CH_3As)_4$ is 83.33 per cent As. The oil distilled mostly below 80° (trimethylarsine boils at 70°).[4] The decomposition of cacodyl at high temperatures is represented by the following equation:

$$4(CH_3)_2AsAs(CH_3)_2 \longrightarrow 4(CH_3)_3As + (CH_3As)_4.$$

That the oil was trimethylarsine was confirmed by the following experiments. Treated with an excess of an aqueous solution of mercuric chloride, a voluminous white precipitate was formed; by recrystallization from hot water, pearly white leaflets were obtained. 0.7070 gram substance gave 0.3918 gram AgCl.

	Calculated for $[(CH_3)_3As]_2HgCl_2$.	Found.
Cl	13.86	13.68

Trimethylarsine-mercuric chloride was formed.

[1] See page 113.
[2] Ann. Chem. (Liebig), **107**, 261. THIS JOURNAL, **35**, 2.
[3] Ann. Chem. (Liebig), **92**, 361; **112**, 228.
[4] Jahres. d. Chem., **1858**, 538.

A chloroform solution of trimethylarsine, treated with a chloroform solution of bromine, evolved much heat and precipitated a heavy, red oil that soon solidified to coarse, red orange, prismatic crystals. The substance was rapidly decomposed by atmospheric moisture and melted at 94°.

0.7088 gram substance gave 0.9481 gram AgBr.

	Calculated for $(CH_3)_2AsBr_3$.	Found.
Br	57.14	56.92

Trimethylarsine dibromide was formed.

III. Reactions of Dimethylarsine.[1]

With BURTON B. WILCOX.

Isoamylene.—When equimolecular quantities of dimethylarsine and isoamylene were heated for one hour at 120°, no change was noticeable. Evidently a reaction indicated in the equation

$$(CH_3)_2AsH + C_5H_{10} = (CH_3)_2(C_5H_{11})As$$

does not take place. The vapor pressures of amylene, methylarsine dichloride, and a mixture of the two in equal volumes were determined; these and other data are given below:

Temperature.	Isoamylene.	CH_3AsCl_2.	Mixture.	Vapor pressure depression.[2]
26.5	531.7	9.0	262.4	260.3
	Amyl chloride.	$AsCl_3$.		
28.5	64.3	11.0	54.9	20.6
	Propyl iodide.	$AsCl_3$.		
28.5	50.1	11.0	24.1	37.0

Benzyl Chloride.—Equimolecular quantities of dimethylarsine and benzyl chloride in ether solution in a sealed tube

[1] Secondary Arsines. Dehn and Wilcox: THIS JOURNAL, **35**, 1–54.

[2] If the depression of vapor pressures of liquid mixtures is an indication of molecular coalescence, then the products

$(CH_3)_2AsH$ Cl_2As Cl_2As

$CH_2{=}CH{-}C_3H_7$ $Cl{-}C_5H_{11}$ $I{-}C_3H_7$

are probably formed, though the molecularly rearranged products

$(CH_3)_2As{-}CH_2{-}CH_2{-}C_3H_7$, $Cl_2As{-}C_5H_{11}$, $ClIAs{-}C_3H_7$,

are not formed.

showed no evidence of reaction, after standing for two months.

Phosphoric Acid.—Equimolecular quantities of dimethylarsine and metaphosphoric acid in a sealed tube showed no evidence of reaction, even after heating for two hours at 95°.

Phenylarsine Dichloride.—When 2.06 grams of dimethylarsine (2 mols.) and 4.3 grams of phenylarsine dichloride (1 mol.) were brought together in a sealed tube filled with carbon dioxide, a dark, red brown solid and *fine, glistening crystals* were formed. Little pressure was observed on opening the tube (absence of hydrogen or hydrochloric acid gas); an ether extract of the contents of the tube, on being filtered and concentrated in a vacuum desiccator, yielded *beautiful, white, compact crystals*, which were immediately decomposed by atmospheric moisture. After washing with a little carbon disulphide, the crystals were dried and quickly analyzed for chlorine. 0.3683 gram of substance gave 0.3058 gram of AgCl.

	Calculated for $(C_6H_5AsCl_2)(CH_3)_2AsH$.	Found.
Cl	21.59	20.57

Dimethylarsinephenylarsine dichloride decomposes rapidly when exposed to the air, precipitating from an ether solution an oil, which was analyzed. 0.2514 gram substance gave 0.1641 gram AgCl.

	Calculated for $C_6H_5AsCl—As(CH_3)_2$.	Found.
Cl	12.00	16.62

The oil was evidently a mixture. The initial reaction of phenylarsine dichloride and dimethylarsine may be expressed thus: $(CH_3)_2AsH$ ‖ $C_6H_5—AsCl_2$.

Diisoamylarsine Chloride.[1]—When equimolecular quantities of dimethylarsine and diisoamylarsine chloride were brought together in a sealed tube filled with carbon dioxide, no change was apparent to the eye, even after heating for five hours at 100°. On opening the tube no pressure (absence of dimethylarsine) was observed; after treating with water, the oil fumed,

[1] Cf. THIS JOURNAL, **35**, 31.

possessed the odor of amylarsine, and undoubtedly was *di-isoamyldimethylcacodyl*. The reaction evidently was as follows:

$$\begin{matrix}(CH_3)_2AsH \\ \| \\ (C_5H_{11})_2AsCl\end{matrix} \rightarrow \begin{matrix}(CH_3)_2As \\ | \\ (C_5H_{11})_2As\end{matrix} + HCl.$$

Propyl Iodide.—When 1.84 grams of dimethylarsine (1 mol.) and 5.83 grams of propyl iodide (2 mols.) were brought together in a sealed tube filled with carbon dioxide and the mixture was allowed to stand for a number of days, a slightly colored oil and some white crystals were formed. On opening the tube, pressure was observed; the crystals, easily decomposed by atmospheric moisture and forming an oil of a tertiary arsine odor, were nearly insoluble in chloroform (all tetralkylarsonium iodides are easily soluble in chloroform). After washing with chloroform they were analyzed with the following results: 0.9038 gram substance gave 0.7651 gram AgI.

	Calculated for $(CH_3)_2(C_3H_7)AsHI$.	Found.
I	46.01	45.75

Some of this *dimethyl-n-propylarsonium iodide* was treated with an excess of isoamyl iodide and heated in a sealed tube for two hours at 120°. The *dimethyl-n-propylisoamylarsonium iodide* was separated by the usual method:

0.6805 gram substance gave 0.4663 gram AgI.

	Calculated for $(CH_3)_2(C_3H_7)(C_5H_{11})AsI$.	Found.
I	36.70	37.03

Diisoamylarsine and n-Propyl Iodide. When 2.5 grams of diisoamylarsine (1 mol.) and 2.8 grams of *n*-propyl iodide (2 mols.) were heated for two hours at 160° in a sealed tube filled with carbon dioxide, a dark red liquid was obtained. On opening the tube, considerable gas was given off; after washing with caustic potash, alcohol, and water, the residual gas gave an excellent test for hydrogen. The product, *diisoamyldi-n-propylarsonium iodide*, was separated in the usual manner and analyzed with the following results: 0.6909 gram substance gave 0.3761 gram AgI.

	Calculated for $(C_5H_{11})_2(C_3H_7)_2AsI$.	Found.
I	29.53	29.42

Cacodyl and Propyl Iodide.—When 4.1 grams of crude cacodyl (1 mol.) and 12.5 grams of *n*-propyl iodide (4 mols.) were heated for 2 hours at 140° in a sealed tube filled with carbon dioxide, a red oil was obtained. After heating with a concentrated solution of potash, filtering, dissolving in chloroform, and reprecipitating with ether, the substance was obtained as yellow crystals. The process of purification was repeated 2 or 3 times but a colorless product could not be separated; after dissolving in a little water, filtering, and evaporating to dryness, light yellow crystals were obtained. 0.6882 gram substance gave 0.4980 gram AgI.

	Calculated for $(CH_3)_2(C_3H_7)_2AsI$.	Found.
I	39.93	39.11

When *dimethyldi-n-propylarsonium iodide* was treated with an excess of mercuric chloride, a white precipitate was formed; after crystallizing from hot water, white leaflets were obtained; 0.2960 gram substance gave 0.2556 gram AgI.2AgCl.

	Calculated for $(CH_3)_2(C_3H_7)_2AsIHgCl_2$.	Found.
I.2Cl	33.59	32.74

Acetyl Iodide and Dimethylarsine.—When equimolecular quantities of acetyl iodide and dimethylarsine were brought together in ether in a sealed tube, an immediate precipitation of a yellow solid and the liberation of considerable heat were observed. After some time the solid changed to a yellow oil and clusters of *needlelike crystals*. After two years, the tube was opened; the ether solution was treated with an aqueous solution of mercuric chloride, when a voluminous white precipitate was formed. After washing with water, alcohol, and ether the substance was analyzed. 0.3803 gram substance gave 0.2756 gram silver halide.

	Calculated for $(CH_3)_2AsH_2O.HgICl$.	Found.
Cl.I	33.51	31.10

The residue in the tube was washed repeatedly with ether and was then dissolved in water and boiled with a solution of mercuric chloride. The odor of acetaldehyde was observed,

while the oil, which was first formed, was slowly changed to mercurous iodide and the double compound with mercuric chloride. The reactions evidently can be represented as follows:

$$(CH_3)_2AsH \longrightarrow \underset{\displaystyle CH_3CO\text{—}I}{\overset{\displaystyle H}{\overset{|}{(CH_3)_2As\text{—}I}}} \longrightarrow (CH_3)_2AsI + CH_3CHO.$$

Chlorcarbonic Ethyl Ester and Dimethylarsine. When equimolecular quantities of the two substances were brought together in a sealed tube filled with carbon dioxide, no reaction was evident to the eye; however, on opening the tube, great pressure (ethyl formic ester boils at 54.4°) and combustible vapors were observed; the residual oil possessed the odor of cacodyl chloride, therefore a reaction had resulted, as follows:

$$(CH_3)_2AsH + ClCOOC_2H_5 \longrightarrow (CH_3)_2AsCl + HCOOC_2H_5.$$

The oil was further identified as cacodyl chloride by shaking its ether solution with an aqueous solution of mercuric chloride —a voluminous white precipitate resulted. The substance was recrystallized from hot water. 0.5451 gram substance yielded 0.3970 gram AgCl.

	Calculated for $(CH_3)_2AsH_2O.HgCl_2$[1].	Found.
Cl	17.98	18.07

Sulphur Dichloride.[2] When 2.13 grams of dimethylarsine (2 mols.) and 2.06 grams of sulphur dichloride (1 mol.) were brought together in a sealed tube containing carbon dioxide, a very violent reaction (much heat) resulted. After standing for two years, a slightly yellow oil, a yellow amorphous solid (sulphur), and *transparent tablets and needles* were observed. On opening the tube a considerable pressure of methyl sulphide (identified by its odor and by the blackening of lead acetate paper) was observed. By heating the tube on the water bath, the liquid distilled out and the crystals increased in quantity (they did not melt at 100°). When treated with ether (evi-

[1] Cf. page 127.
[2] Cf. THIS JOURNAL, 35, 38.

dently containing a little water) the crystals were decomposed, thereby giving rise to the odor of cacodyl chloride and precipitating finely divided sulphur. A chloroform solution of the crystals standing in a desiccator deposited sulphur. These crystals were not analyzed; that they are an *intermediate* product in the following reaction is sufficiently evident:

$$2(CH_3)_2AsH + SCl_2 \longrightarrow 2(CH_3)_2AsCl + S.$$

Arsenic Trioxide.—When 1.7 grams of dimethylarsine (3 mols.) and 2.1 grams of arsenic trioxide (2 mols.) were brought together in a sealed tube filled with carbon dioxide, a very slow reaction ensued—a dark brown solid gradually replaced the trioxide. The tube was heated for five hours at 100° and then was permitted to stand for two years; on opening the tube some unchanged arsine but no arsenic trioxide was observed. The red brown solid was analyzed.

0.1246 gram substance gave 0.2137 gram $Mg_2As_2O_7$.
0.1046 gram substance gave 0.1790 gram $Mg_2As_2O_7$.

	Calculated for $As_2O_3(CH_3As)_4$.	Calculated for $(CH_3As)_4$.	Found. I.	Found. II.
As	75.75	83.33	82.99	82.80

Evidently the reaction is largely as follows:

$$2(CH_3)_2AsH + As_2O_3 = (CH_3As)_4 + H_2O + O_2.$$

Arsenic Trichloride.[1]—When 3 grams of dimethylarsine (2 mols.) and 2.56 grams of arsenic trichloride (1 mol.) were brought together in ether in a sealed tube, a dark brown solid was precipitated at once. After standing for two years the ether solution was poured out; the amorphous brown solid was seen to be mixed with *long, prismatic, transparent crystals*, which were decomposed rapidly by contact with the atmosphere, hence they were not separated and analyzed. Evidently they were an *intermediate compound*. The red brown substance was washed with dilute hydrochloric acid and analyzed:

0.2453 gram substance gave 0.4238 gram $Mg_2As_2O_7$.

	Calculated for $(CH_3As)_4$.	Found.
As	83.33	83.60

[1] Cf. This Journal, **35**, 40.

The ether solution was treated with an aqueous solution of mercuric chloride; the voluminous white precipitate was recrystallized from hot water and analyzed.

0.6630 gram substance gave 0.4800 gram AgCl.

	Calculated for $(CH_3)_2AsH_2OHgCl_2$[1].	Found.
Cl	17.98	17.87

Evidently the end reaction is as follows:

$$4(CH_3)_2AsH + 2AsCl_3 = (CH_3As)_4 + 2(CH_3)_2AsCl + 4HCl$$

URBANA, ILLINOIS,
August 5, 1907.

REVIEWS.

A TEXT-BOOK OF ORGANIC CHEMISTRY. By A. F. HOLLEMAN, PH.D., F. R. A. Amst., Professor Ordinarius in the University of Amsterdam. Translated from the Third Dutch Edition by A. JAMIESON WALKER, PH.D. (Heidelberg), B. A., Head of the Department of Chemistry, Technical College, Derby, England. Assisted by OWEN E. MOTT, PH.D. (Heidelberg). Second English Edition, Rewritten. New York: John Wiley and Sons; London: Chapman and Hall, Limited. 1907. Price, $2.50.

The author states that he has rewritten the chapter on pyrrol and that instead of giving prominence to any one formula for benzene he has presented the formulae of Kekulé, von Baeyer, and Thiele side by side. The treatment is otherwise similar to that in former editions.

The reviewer welcomes the use, in this book, of physical-chemical theories in the explanation of organic reactions. Such a large mass of facts connected with catalysis, tautomerism, and alkylation reactions is now known that there is a real demand for a text on physico-organic chemistry.

This new edition should receive the hearty reception given the former ones.

S. F. ACREE.

[1] Bunsen (Ann. Chem. (Liebig), **37**, 50) prepared from cacodylic oxide and mercuric chloride a white crystalline compound that seems to be identical with the above described substance, prepared from cacodyl chloride and mercuric chloride. Bunsen's analytical data agree more closely with the formula $(CH_3)_2AsHgCl.H_2O$ than with $[(CH_3)_2As]_2O.2HgCl$, which he assigned to the compound.

	Found. Bunsen	$(CH_3)_2AsHgCl_2.H_2O$.	Calculated for $(CH_3)_2AsO.HgCl_2$.	$[(CH_3)_2AsH]_2O.2HgCl_2$
C	6.23	6.09	6.12	6.25
H	1.76	2.03	1.54	1.56
As	19.25	19.04	19.14	19.54
O	3.94	4.06	4.08	2.08
Hg	50.80	50.79	51.04	52.11
Cl	18.02	17.98	18.07	18.45

ORGANIC CHEMISTRY, Including Certain Portions of Physical Chemistry, for Medical, Pharmaceutical, and Biological Students (With Practical Exercises). By H. D. HASKINS, A.B., M.D., Instructor in Organic and Biochemistry, Medical Department, Western Reserve University, and Professor of Chemistry, Cleveland School of Pharmacy, and J. J. MACLEOD, M.B. (Aberd.), D.PH. (Camb.), Professor of Physiology, Western Reserve University. First Edition. New York: John Wiley and Sons; London: Chapman and Hall, Limited. 1907. Price, $2.

The authors state in the preface that this little book is written to present to biochemical students an outline of that part of organic chemistry which is most useful to them and to acquaint them with the physical-chemical conceptions and methods which are now of great importance. The text contains a large number of well selected experiments, and there are some useful tables at the end. An excellent feature of the book is the presentation of the graphical formulae of the important compounds in the sugar, alkaloid, and other groups.

S. F. ACREE.

EXERCISES IN ELEMENTARY QUANTITATIVE CHEMICAL ANALYSIS FOR STUDENTS OF AGRICULTURE. By AZARIAH THOMAS LINCOLN, PH.D., and JAMES HENRI WALTON, JR., PH.D., Assistant Professor of Chemistry, University of Wisconsin. New York: The Macmillan Co. 1907. pp. xv + 218. Price, $1.25.

This excellent manual presents a series of exercises designed particularly for the student of agriculture, by means of which he is taught the fundamental methods of quantitative chemical analysis as applied to a considerable range of inorganic substances of common occurrence and to those operations which are more directly typical of agricultural analysis. Representative procedures of gravimetric and volumetric analysis are included under the former category, and the methods for the analysis of milk, butter, cereals, fertilizers, and soils under the latter. A carefully written chapter on Stoichiometry follows, and the appendix contains a variety of useful information and a series of tables.

Under the plan adopted throughout the book, the procedures are given in considerable detail, and are followed by a series of explanatory notes, and references, to works of larger scope, or to articles in the journals which bear upon the methods described. With the usual allowance for necessary differences of opinion regarding the selection of a particular procedure, or the relative emphasis to be placed on a particular point, the manual appears to be worthy of hearty commendation. The typography is excellent and the text shows evidence of careful preparation.

H. P. TALBOT.

TRAITÉ COMPLET D'ANALYSE CHIMIQUE APPLIQUÉE AUX ESSAIS INDUSTRIELS. Par J. POST et B. NEUMANN. Deuxième édition française entierement refondue. Traduite d'après la troisième édition allemande et augmentée de nombreuses additions par le DR. L. GAUTIER Tome second, premier fascicule. Paris: Librairie Scientifique A. Hermann. 1908. pp. 199. Price, Fr. 6.

This is a faithful reproduction of the German edition noted in the title above. The additions consist chiefly of certain specifications regarding cements taken from the Annales des Ponts et Chaussées. The German edition has already been noticed in THIS JOURNAL. H. P. TALBOT.

DAIRY LABORATORY GUIDE. By CHARLES W. MELICK, B.S.A., M.Sc., Professor of Dairy Husbandry, Maryland Agricultural Experiment Station. Illustrations, 52. New York: D. Van Nostrand Company. 1907. pp. 129. Price, $1.25.

As its name indicates this book is a guide for the dairy laboratory and not for the laboratory of dairy chemistry. It is brief and condensed in its presentation of the subject and does not pretend to describe apparatus or to explain the principles of the processes considered. Its object is to give in systematic order the various operations of a dairy or creamery and with them some of the simpler chemical and bacteriological tests. The arrangement of the book is good and it is well written and printed.

For the student under the direction of an instructor and in a laboratory where the various forms of apparatus mentioned are in use, it will serve as an aid in directing and systematizing the work. It cannot, however, be used with profit by any one outside of a laboratory of instruction.

The book covers considerable ground and presents for study the more common operations in the handling of milk and the manufacture of milk products. It also contains sections dealing with mechanical contrivances, repair of machinery, modified milk, standardized milk, condensed milk, refrigeration, pasteurization and receipts for various materials made from milk. There are a few misstatements and typographical errors, but these are neither numerous nor serious in nature.

J. S. C.

MEMENTO DU CHIMISTE (ancien Agenda du Chimiste). Recueil de tables et de documents divers indispensables aux laboratoires officiels et industriels, publié sous la direction de A. HALLER, Membre de l'Institut, et CH. GIRARD, Directeur du Laboratoire Municipal de Paris. Paris: H. Dunod et E. Pinat. 1907. xx + 758 pp. Price, Fr. 12.

This book marks the revival, under a somewhat modified form, of the "Agenda du Chimiste" which appeared annually

from 1877 to 1897. It is similar in character to Biedermann's well-known "Chemiker Kalender," but is printed in larger and clearer type. The first 172 pages contain various mathematical and physical tables, 190 pages are given to analytical data and to the formulas and principal physical properties of inorganic and organic compounds and of minerals, and the balance of the book is devoted to information concerning applied and industrial chemistry. A portrait of Charles Friedel and a brief sketch of the life and work of this chemist are given in the introduction. Every laboratory worker will find this a very useful book to have on his table. C. A. R.